UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OPP OFFICIAL RECORD
HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS
EPA SERIES 361

OFFICE OF PREVENTION, PESTICIDE AND TOXIC SUBSTANCES

MEMORANDUM

Date: 22 October 2009

SUBJECT: Endothall; Petition for Tolerances on Irrigated Crops. Summary of Analytical Chemistry and Residue Data.

PC Codes: 038901, 038904 and 038905	**DP Barcode:** 356315
Decision No.: 399181	**Registration Nos.:** 70506-175 and 70506-176
Petition No.: 8E7419	**Regulatory Action:** Section 3
Risk Assessment Type: NA	**Case No.:** 2245
TXR No.: NA	**CAS Nos.:** 145-73-3; 2164-07-0; 66330-88-9
MRID No.: See MRID Summary Table	**40 CFR:** 180.293

Ver.Apr.08

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MRID Summary Table		
MRID No.	**Study Type**	**Comments**
47520701	860.1400 Irrigated Crops (Root & Tuber Vegetables)	New DERs, 47520701.de1 (sugar beet, carrot and potato field trials) and 47520701.de2 (sugar beet processing study)
47520702	860.1400 Irrigated Crops (Bulb Vegetables)	New DERs, 47520702.de1 (onion field trials)
47520703	860.1400 Irrigated Crops (Leafy Vegetables)	New DER, 47520703.der (lettuce field trials)
47520704	860.1400 Irrigated Crops (Brassica Leafy Vegetables)	New DER, 47520704.der (cabbage field trials)
47520705	860.1400 Irrigated Crops (Legume Vegetables)	New DER, 47520705.de1 (pea, bean and soybean field trials) and 47520705.de2 (soybean processing study)
47520706	860.1400 Irrigated Crops (Fruiting Vegetables)	New DERs, 47520706.de1 (tomato field trials) and 47520706.de2 (tomato processing study)
47520707	860.1400 Irrigated Crops (Cucurbit Vegetables)	New DER, 47520707.der (cucumber field trials)
47520708	860.1400 Irrigated Crops (Citrus Fruits)	New DER, 47520708.de1 (orange field trials) and 47520708.de2 (orange processing study)
47520709	860.1400 Irrigated Crops (Pome Fruit)	New DERs, 47520709.der (apple field trials) and 47520709.de2 (apple processing study)
47520710	860.1400 Irrigated Crops (Stone Fruit)	New DER, 47520710.der (peach field trials)
47520711	860.1400 Irrigated Crops (Berry Group)	New DER, 47520711.der (blueberry and blackberry field trials)
47520712	860.1400 Irrigated Crops (Tree Nut Group)	New DER, 47520712.der (almond and pecan field trials)
47520713	860.1400 Irrigated Crops (Cereal Grain)	New DER, 47520713.de1 (corn, sorghum and wheat field trials) and 47520713.de2 (corn, sorghum and wheat processing studies)
47520714	860.1400 Irrigated Crops (Grass)	New DER, 47520714.der (grass field trials)
47520715	860.1400 Irrigated Crops (Nongrass animal feeds)	New DER, 47520715.der (alfalfa field trials)
47520716	860.1400 Irrigated Crops (Grapes)	New DER, 47520716.de1 (grape field trials) and 47520716.de2 (grape processing study)
47520717	860.1400 Irrigated Crops (Mint)	New DER, 47520717.de1 (mint field trials) and 47520707.de2 (mint processing study)
47520718	860.1400 Irrigated Crops (Rice)	New DER, 47520718.de1 (rice field trials) and 47520718.de2 (rice processing study)
47520719	860.1380 Storage Stability (Various Crops)	New DER, 47520719.der (plant storage stability data)

This document was originally prepared under contract by Dynamac Corporation (1910 Sedwick Road, Building 100, Suite B; Durham, NC 27713). The document has been reviewed by the Health Effects Division (HED) and revised as needed for clarity, correctness, and to reflect current Office of Pesticide Programs (OPP) policies.

Executive Summary

Endothall is a selective contact herbicide, defoliant, desiccant, and aquatic algaecide belonging to the dicarboxylic acid chemical class. The free acid of endothall and its dipotassium and mono-N,N-dimethylalkyl-amine salts (monoalkylamine) are registered in the United States primarily as aquatic herbicides for the control of a variety of plants in water bodies. This includes irrigation canals, but only with a 7 day holding period. Endothall is also registered for desiccation/de-foliation of alfalfa/clover (grown for seed only), cotton, and potatoes prior to harvest, and for reduction of sucker branch growth in hops. Permanent tolerances have been established for the combined residues of endothall and its monomethyl ester at 0.1 ppm in/on cotton seeds, fish, dried hops and potatoes, and at 0.05 ppm in/on rice grain and straw [40 CFR §180.293(a)(1)]. An interim tolerance of 0.2 ppm has also been established for endothall, *per se*, in potable water resulting from the use of the monoalkylamine or dipotassium salts of endothall for control of aquatic plants in canals, lakes, ponds and other potential water sources. An interim tolerance has also been established for endothall on sugar beet at 0.2 ppm [40 CFR §180.319].

There are currently three endothall end-use products registered to United Phosphorus, Inc. (UPI) for control of algae and aquatic weeds in drainage and irrigation canals, including two monoalkylamine salt formulations and a dipotassium salt formulation. The monoalkylamine salt of endothall is formulated as either a 2 lb ae/gal SC/L formulation (EPA Reg. No. 70506-175) or an 11% granular (G) formulation (EPA Reg. No. 70506-174), containing 5% ae. The dipotassium salt is formulated as a 4.23 lb ai/gal SC/L (EPA Reg. No. 70506-176), which is equivalent to 3.0 lb ae/gal SC/L. [In order to avoid the complications of different molecular weights for different salts, endothall concentrations are expressed as the free acid equivalents (ae).] Labels for these products allow for repeated broadcast applications to irrigation canals at rates yielding endothall concentrations of up to 5 ppm ae for the monoalkylamine salt and 3.5 ppm ae for the dipotassium salt. The labels do not currently specify a maximum number of applications per season or a maximum seasonal use rate. Depending on the concentration in the treated water, the use directions specify minimum holding times of 7 days (0.3 ppm rate) to 25 days (5 ppm rate) prior to using the treated water for irrigation of crops.

Interregional Research Project No. 4 (IR-4) has proposed amending the use directions for the 2 lb ae/gal SC/L monoalkylamine salt and the 3 lb ae/gal dipotassium salt of endothall to remove the holding times after water is treated with endothall before it can be used to irrigate crops, which would enable use of endothall on moving water in canals etc, and would effectively create a zero day PHI. The amended uses specify minimum retreatment interval (RTI) of 7 days for irrigation canals and a maximum seasonal use rate of 30 ppm ae per season (6 applications at up to 5 ppm ae/application). In conjunction with the proposed amendments, IR-4 has proposed the following tolerances for indirect or inadvertent residues of endothall on irrigated crops:

Vegetable, root and tuber, group 1 .... 2 ppm
Vegetable, leaves of root and tuber, group 2 .... 3.5 ppm
Vegetable, bulb, group 3-07 .... 2 ppm
Vegetable, leafy, except Brassica, group 4 .... 3.5 ppm
Vegetable, Brassica, leafy, group 5 .... 0.1 ppm
Vegetable, legume, group 6 .... 3 ppm
Vegetable, fruiting, group 8 .... 0.05 ppm
Vegetable, cucurbit, group 9 .... 1.1 ppm
Fruit, citrus, group 10 .... 0.05 ppm
Fruit, pome, group 11 .... 0.05 ppm
Fruit, stone, group 12 .... 0.25 ppm
Berry and small fruit, group 13-07 .... 0.6 ppm
Nut, tree, group 14 .... 0.05 ppm
Almond, hulls .... 10 ppm
Grain, cereal, group 15 .... 2.5 ppm
Grain, cereal, forage, fodder and hay, group 16, forage .... 3.5 ppm
Grain, cereal, forage, fodder and hay, group 16, hay .... 5 ppm
Grain, cereal, forage, fodder and hay, group 16, stover .... 11 ppm
Grain, cereal, forage, fodder and hay, group 16, straw .... 6 ppm

Grain, aspirated fractions ....24 ppm
Grass, forage fodder, and hay, group 17, forage ....3 ppm
Grass, forage fodder, and hay, group 17, hay....................19 ppm
Nongrass animal feed, group 18, forage ....3.5 ppm
Nongrass animal feed, group 18, hay....................8 ppm
Grape....................0.9 ppm
Peppermint tops ....7 ppm
Spearmint tops ....7 ppm
Rice, grain....................1.7 ppm
Rice, straw....................4.5 ppm

The qualitative nature of endothall residues in plants is adequately understood based upon the metabolism studies on alfalfa, cotton and sugar beets. The qualitative nature of endothall residues in livestock is also understood based upon the adequate goat and poultry metabolism studies. The Agency has concluded that endothall and its monomethyl ester are the residues of concern in both plant and animal commodities for purposes of the tolerance expression and risk assessment. The residue of concern in water is only endothall.

A GC method with microcoulometric nitrogen detection is listed as Method I in the Pesticide Analytical Manual (PAM, Volume II) for determining endothall residues in/on crop commodities, and a confirmatory HPLC/MSD method (Method No. KP218R0) is also available for determining residues of endothall and its monomethyl ester in fish and residues of endothall in plant commodities. For the irrigated crop field trails and processing studies submitted with the current petition, endothall residues in/on plant commodities were determined using an adequate LC/MS/MS method (Method No. KP-242R1). For this method, residues are extracted with water and then derivatized with heptafluoro-*p*-tolylhydrazine (HFTH) in 50% H_3PO_4. The derivatized residues are cleaned up by solvent partitioning and elution through a solid phase extraction (SPE) cartridge. Residues are then analyzed by LC/MS/MS using external standards for quantitation. Residues are expressed in endothall acid equivalents, and the validated limit of quantitation (LOQ) for endothall is 0.05 ppm for plant commodities.

Adequate storage stability data are available supporting the sample storage conditions and durations for the irrigated crop field trials and processing studies. The newly submitted storage stability data indicate that endothall is stable for up to 15 months in frozen tomatoes, lettuce, sugar beet roots, and corn grain and for up to 10 months in soybean seeds and oil.

The submitted field trial data on irrigated crops were conducted according to the previously submitted protocol. Two to four field trials were conducted on each of the following crops in their major growing regions: potato, carrot, sugar beet, green and bulb onions, leaf and head lettuce, cabbage, succulent podded peas and beans, dry beans, soybean, tomato, cucumber, orange, apple, peach, blueberry, blackberry, grape, pecan, almond, field and sweet corn, sorghum, wheat, rice, alfalfa, grasses and mint. These crops were selected to represent the major crop groups. In each field trial, the monoalkylamine salt of endothall (2 lb ae/gal SC/L) was used to treat the irrigation water at a rate of ~5 ppm ae, and the treated water was then applied via overhead sprinklers as six broadcast foliar applications at RTIs of 5-10 days. [The target application volume in each trial was equivalent to ~1 acre inch of water (27,154 gal/A). Based on the concentration of the endothall in the irrigation water and the amount of water applied, the application rates for endothall were equivalent to 1.10-1.25 lb ae/A/application, for totals of 5.64-7.17 lb ae/A/season.] We note that each field trial comprised only a single plot that was then sampled twice to provide two results.

With only a few exceptions, samples of the regulated raw agricultural commodities (RACs) from each crop were harvested on the day of the sixth application (0 days after treatment, DAT). The 0 DAT exceptions comprise soybean seed harvested from one plot at 1 DAT, wheat grain and straw (and also the source of the aspirated grain fraction result) harvested from one plot at 1 DAT, rice grain and straw harvested from one plot at 1 DAT, some of the grass samples harvested at 1 – 2 DAT. (Interestingly, much higher results were found for the single soybean seed and single wheat grain samples harvested at 1 DAT than for the other soybean samples and wheat grain samples harvested at 0 DAT. This was not true for rice.) In addition, in the field corn, sorghum and wheat field trials, samples of forage and hay (wheat only) were collected at 0 DAT, but following only 2 or 3 applications of endothall treated water.

Side-by-side tests were also conducted on some of these crops (sugar beets, lettuce, cucumber, and peaches) comparing application of the dipotassium salt of endothall (3 lb ae/gal SC/L) with the monoalkylamine salt. Although the dipotassium salt was applied to the irrigation water following the label directions for that salt, the resulting concentration of endothall in the water was 3.5 ppm ae (0.7x rate). [The application rates for the dipotassium salt were equivalent to 0.74-091 lb ae/A/application, for totals of 4.67-5.07 lb ae/A/season.]

Several deficiencies were noted in the field trials (see below), but the submitted field trial data can generally be considered adequate for assessing inadvertent residues of endothall on irrigated crops. Results should be very conservative.

The residues determined in the 0 DAT samples should represent an over-estimate of residues for many of the crops tested because irrigation on the day of harvest would be highly unlikely to occur in commercial harvesting procedures. Crops and commodities which would be unlikely to be irrigated just prior to harvest include: sugar beets, carrots, potatoes, dry bulb onions, dried peas and beans, soybeans, tree nuts, field corn grain and stover, sorghum grain and stover, wheat grain and straw, and rice grain and straw.

Also, all crops were overhead irrigated. For grapes at least, according to BEAD, the vines may be overhead irrigated when not in fruit, as in these trials, but are usually only irrigated by drip irrigation once in fruit, to reduce the growth of mold on the grape. In addition, HED notes that phytotoxicity was reported on a number of the crops tested, including legume vegetables, cucumbers, apple trees, peach trees, grape vines, mint and grass. The phytotoxicity generally appeared beginning after the second application and consisted of leaf chlorosis and necrosis, with some crops also having reduced growth and stunting. The occurrence of phytotoxicity on a wide range of crops suggests that repeated irrigation with water containing high levels (5 ppm) endothall is unlikely to occur undetected under normal agricultural conditions. Finally, of course, the application rate used was, appropriately, at the maximum permitted rate, and the number of applications at the high end of the number of treatments expected in a season. As always, it is expected that the maximum rate and maximum number of treatments will not be often used.

Adequate processing studies were submitted for all possible irrigated crops, with the exception of oil seed crops and processing of grapes to grape juice. Although no processing data were submitted for any crops in the "Oilseeds Crop Group", the available soybean processing study can serve that purpose in this case and indicates that endothall residues are unlikely to concentrate in either oilseed meal or refined oil. Because there were problems in study for processing grapes into grape juice, a maximum theoretical processing factor of 1.2x has been used in place of the study data. Grape juice can therefore take the same tolerance as grapes.

Based on the highest average field trial (HAFT) residues for the various irrigated crops and the observed processing factors, separate tolerances are required for the following processed commodities at the recommended levels: apple wet pomace (0.15 ppm), raisins (3 ppm), dried citrus pulp (0.1 ppm), rice hulls (5 ppm), soybean hulls (0.3 ppm), sugar beet molasses (1.2 ppm), tomato paste (0.1 ppm), and wheat milled byproducts (5 ppm). The wheat grain processing study also indicates that endothall residues can concentrate in aspirated grain fractions (AGF) by 15x. Based on the HAFT residues for wheat grain, which were the highest for all grains, an appropriate tolerance for AGF would be 30 ppm.

No cattle and poultry feeding studies have been submitted for endothall. Considering the exposure of livestock to endothall residues through both the consumption of feedstuffs from irrigated crops and from the drinking of endothall treated water treated at 5 ppm endothall ae, the calculated maximum dietary exposure of livestock to endothall is 27.7 ppm for beef cattle, 35.8 ppm for dairy cattle, 16.8 ppm for poultry, and 19.7 ppm for swine.

Proposed tolerances in meat tissues have therefore been based upon these dietary burdens and upon the TRR developed in the meat tissues when goats and chickens were fed radiolabeled endothall for the metabolism studies. Approval will require confirmatory submission of the required feeding studies.

The Agency has concluded that the only residues of significance in rotated crops are endothall and its monomethyl and dimethyl esters. Although data from limited field rotational crop trials have been previously required, the inadvertent exposure of crops to endothall via the use of treated irrigation water will exceed the potential exposure of crops from being planted in rotation with endothall treated primary crops. Therefore, the establishment of tolerances for indirect/inadvertent residues of endothall on the proposed irrigated crops precludes any further need for limited field rotational trial data or for rotational crop tolerances.

Regulatory Recommendations and Residue Chemistry Deficiencies

Several deficiencies were noted in the subject petition, but none of these would preclude establishing permanent tolerances for inadvertent endothall residues in/on irrigated crop commodities. Although the following deficiencies were noted in the irrigate crop field trials, no action is required to resolve these deficiencies.

- The bridging studies comparing the use of the monoalkylamine and dipotassium salts of endothall were of limited use as the two formulations were applied at different rates. In terms of acid equivalents, the monoalkylamine salt was applied at a concentration of 5 ppm and the dipotassium salt was applied at a concentration of 3.5 ppm, which is the maximum allowed use rate of the dipotassium salt (0.7x rate for the monoalkylamine salt). For each of the crops tested with both salt formulations, endothall residues were 0.6-0.9x lower for the dipotassium salt than for the monoalkylamine salt, which is consistent with the lower use rate for the dipotassium salt. Although the bridging studies do not allow for direct comparison of the two salts, the data do indicate that endothall residues resulting from application of the dipotassium salt to irrigation canals would generally be expected to be lower than from the monoalkylamine salt, when both are applied according to current label directions.

- Spinach should have been used as the representative leafy vegetable crop, as foliar applications generally result in higher residues on spinach than on lettuce (leaf and head) or celery.

- Mustard greens should have been used as the representative Brassica vegetable crop, as foliar applications generally result in higher residues on mustard greens than on broccoli, cauliflower or cabbage.

- Field corn forage, sorghum forage and wheat forage and hay only received 2-3 applications prior to harvest. For these crops, separate plots should have been established for collection of forage and hay samples so that all six applications could have made prior to harvest of forage and hay.

- No field trials were conducted on an oil seed crop such as, canola, flax, safflower, or sunflower.

- No field trials were conducted on peanuts, which is a major field crop.

The following additional deficiencies were also noted in the submitted petition; however, these deficiencies must be resolved as a condition of registration.

- Data are required indicating whether or not the submitted LC/MS/MS method is capable of extracting and recovering the monomethyl ester of endothall.

- Dairy cattle and laying hen feeding studies are required to support immediate application of endothall-treated irrigation water to crops.

- A revised Section F is required including the recommended tolerances on RACs and processed commodities from irrigated crops.

HED recommends for establishing permanent tolerances for indirect or inadvertent residues of endothall on irrigated crops. The recommended tolerances for the various crops and crop groups and their associated processed commodities are listed in Table 10. The tolerances for irrigated crops should be established under 40 CFR §180.293(d). A human health risk assessment for endothall is forthcoming.

Background

Endothall is a dicarboxylic acid that is a selective contact herbicide, defoliant, desiccant, and aquatic algaecide. The free acid of endothall (PC Code 038901) and its dipotassium (PC Code 038904) and monoalkylamine (PC Code 038905) salts are registered primarily as aquatic herbicides for the control of a variety of plants in water bodies, including irrigation canals. However, these uses require a minimum 7 day holding period before the water can be used on crops. They are also registered for desiccation/ defoliation of alfalfa/clover (grown for seed only), cotton, and potatoes prior to harvest, and for reduction of sucker branch growth in hops. The Reregistration Eligibility Decision (RED) for endothall was issued September 2005.

Permanent tolerances are established for the combined residues of endothall and its monomethyl ester at 0.1 ppm in/on cotton seeds, dried hops and potatoes, and at 0.05 ppm in/on rice grain and rice straw [40 CFR §180.293(a)(1)]; and an interim tolerance has also been established for endothall on sugar beet at 0.2 ppm [40 CFR §180.319]. These tolerances are intended to cover intended direct use of endothall on these crops. Permanent tolerances are also established for fish at 0.1 ppm straw [40 CFR §180.293(a)(1)].

Residue data supporting irrigation of crops with endothall treated water were previously submitted using cabbage, celery, grapefruit, peppers and turnips as representative crops. However, these studies were deemed inadequate to support the establishment of crop group tolerances. Additional data were required for other representative crop group commodities and the irrigated crop studies were conducted using endothall in the water at 3 ppm, which is 0.6x the maximum application rate of 5 ppm for aquatic sites. The Endothall RED reiterated the need for extensive crop field trials to support the use of treated irrigation water on crops. The application rate in these tests needed to reflect the maximum aquatic use rate of endothall (5 ppm) and the maximum possible number of applications per season.

In response to the above requirements, IR-4 has proposed amendments to the use directions for endothall on irrigation canals and has submitted extensive crop field trials to support tolerances on irrigated crops (PP#8E7419) when endothall is used with a zero day holding period. The chemical structure and nomenclature of endothall and its salts are listed in Table 1. The physicochemical properties of technical grade endothall and its salts are listed in Table 2.

Table 1. Structure and Nomenclature of Endothall and its Salts.

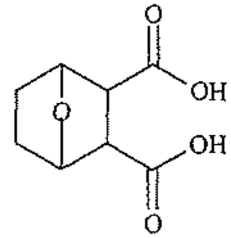
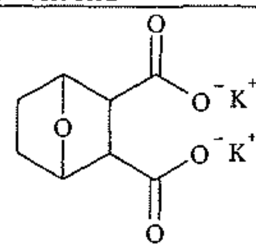
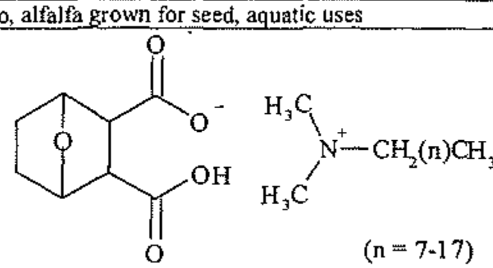
Chemical Structure	
Common name	Endothall
Molecular Formula	$C_8H_{10}O_5$
Molecular Weight	186.16
IUPAC name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid
CAS name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid
CAS #	145-73-3
PC Code	038901
Current Food/Feed Site Registration	Cotton, hops, potato, alfalfa grown for seed
Chemical Structure	
Common name	Endothall, dipotassium salt
Molecular Formula	$C_8H_8K_2O_5$
Molecular Weight	262.33
IUPAC name	Not available
CAS name	Not available
CAS #	2164-07-0
PC Code	038904
Current Food/Feed Site Registration	Cotton, hops, potato, alfalfa grown for seed, aquatic uses
Chemical Structure	 (n = 7-17)
Common name	Endothall, mono-N,N-dimethylalkyl amine salt
Molecular Formula	Not available
Molecular Weight	Average: 422
IUPAC name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid, compound with N,N-dimethylcocoamine
CAS name	Not available
CAS #	66330-88-9
PC Code	038905
Current Food/Feed Site Registration	Cotton, hops, potato, alfalfa grown for seed, aquatic uses

Table 2. Physicochemical Properties of Endothall and its Salts.		
Parameter	Value	Reference
Endothall (acid)		
Melting point	108-110°C	DP# 304026, D. Soderberg, 6/10/2004
pH	2.7 at 25°C (1% solution)	
Density, bulk density, or specific gravity	0.481 g/cm^3 (bulk) at 25°C	
Water solubility at 25°C	109.8 g/L 13.1 g/100 mL in water, pH 5 12.7 g/100 mL in water, pH 7 12.5 g/100 mL in water, pH 9	
Solvent solubility at 25°C	3.4 g/100 mL in acetonitrile 2.4 g/100 mL in n-octanol 16.0 g/100 mL in tetrahydrofuran	
Vapor pressure	3.92 x 10^{-5} mm Hg at 24.3°C	
Dissociation constant, pK$_a$	4.32 for Step 1 and 6.22 for Step 2 at 20°C (0.2% solution in 20% basic ethanol); dissociation rate 1.8-2.3 x 10^3 μmho within 3-5 minutes at □25°C, by conductivity meter	
Octanol/water partition coefficient	Not applicable to endothall acid	
UV/visible absorption spectrum	Not available	
Endothall, dipotassium salt		
Melting point	>360°C	DP# 304026, D. Soderberg, 6/10/2004
pH	9.1 at 25°C (1% solution)	
Density, bulk density, or specific gravity	0.766 g/cm^3 (bulk) at 25°C	
Water solubility	>65 g/100 mL in water, pH 5, pH 7, and pH 9	
Solvent solubility	<0.001 g/100 mL in acetonitrile, n-octanol, and tetrahydrofuran	
Vapor pressure	Not applicable. An organic acid K salt is anticipated to have an insignificant vapor pressure.	
Dissociation constant, pK$_a$	4.16 for Step 1 and 6.14 for Step 2 at 20°C in water; dissociation complete at 5 mins (13.6 x 10^3 μmho)	
Octanol/water partition coefficient	K_{OW} <0.02 and <0.3 at concentrations of 9 x 10^{-3} M and 9 x 10^{-4} M, respectively, at 25°C	
UV/visible absorption spectrum	Not available	
Endothall, mono-N,N-dimethylalkyl amine salt		
Boiling point	Not available	DP# 304026, D. Soderberg, 6/10/2004
pH	5.2 at 25°C (1% solution)	
Density, bulk density, or specific gravity	1.028 g/mL at 25°C	
Water solubility at 25°C	≥49.2 g/100mL in water, pH 5 ≥51.6 g/100 mL in water, pH 7 ≥49.8 g/100 mL in water, pH 9	
Solvent solubility at 25°C	≥102.5 g/100mL in acetonitrile ≥95.4 g/100 mL in n-octanol ≥104.3 g/100 mL in tetrahydrofuran	
Vapor pressure	2.09 x 10^{-5} mm Hg at 25°C (calculated; mixed mono- and dialkylamine (C8-C20))	
Dissociation constant, pK$_a$	4.24 for Step 1 and 6.07 for Step 2 at 20°C for mixed mono- and dialkylamine (C8-C20) in acidified ethanol/water; dissociation complete □17 minutes (1.7 x 10^3 μmho) at 25°C	
Octanol/water partition coefficient	K_{OW} 2.097 at concentrations of 8.9 x 10^{-3} M and 8.9 x 10^{-4} M, at 25°C	
UV/visible absorption spectrum	Not available	

860.1200 Directions for Use

There are currently three endothall end-use products registered to UPI for control of algae and aquatic weeds in drainage and irrigation canals, including two monoalkylamine salt formulations and a dipotassium salt formulation. The monoalkylamine salt of endothall is formulated as either a 2 lb ae/gal SC/L formulation (Hydrothol 191; EPA Reg. No. 70506-175) or an 11% G formulation (Hydrothol Granular; EPA Reg. No. 70506-174), which contains 5% acid equivalent of endothall. The dipotassium salt is formulated as a 4.23 lb ai/gal SC/L (Aquathol® K; EPA Reg. No. 70506-176), which is equivalent to 3.0 lb ae/gal SC/L.

The current labels for these products allow for repeated broadcast applications to irrigation canals at rates yielding endothall concentrations of up to 5 ppm ae for the monoalkylamine salts and 3.5 ppm ae for the dipotassium salt. (HED notes that the label directions for the dipotassium salt are expressed in lb ai rather than lb ae; therefore the use rates for the dipotassium salt are ~0.7x the use rates for the monoalkylamine salt.) The labels do not currently specify a maximum number of applications per season or a maximum seasonal use rate. Depending on the concentration in the treated water, the use directions specify minimum holding times of 7 days (0.3 ppm rate) to 25 days (5 ppm rate) prior to using the treated water for irrigation of crops.

IR-4 is supporting an amendment to the use directions for the 2 lb ae/gal SC/L monoalkylamine salt and the 3 lb ae/gal SC/L dipotassium salt of endothall to remove the holding time restriction for using endothall-treated water from irrigation canals for the irrigation of crops. The amended uses also specify a minimum RTI of 7 days and a maximum seasonal use rate of 30 ppm ae per season. Example labels containing the proposed use directions were provided and are summarized below in Table 3.

Table 3. Summary of Proposed Use Directions for Endothall Salts on Irrigation and Drainage Canals.

Applic. Timing, Type, and Equip.	Formulation [1] [EPA Reg. No.]	Applic. Rate [2]	Maximum Seasonal Rate [2]	PHI (days)	Use Directions and Limitations
Endothall Monoalkylamine Salt (PC Code 038905)					
Broadcast surface application to water; ground equipment	2.0 lb ae/gal SC/L [70506-175]	5.0 ppm	30 ppm	0 [3]	A minimum 7-day RTI is specified. Do not use treated water for domestic purposes or animal consumption within the following period: 0.3 ppm - 7 DAT; 3.0 ppm - 14 DAT; and 5.0 ppm - 25 DAT.
Endothall dipotassium salt (PC Code 038904)					
Broadcast surface application to water; ground equipment	3.0 lb ae/gal SC/L [70506-176]	3.5 ppm	21 ppm	0 [3]	A minimum 7-day RTI is specified. Do not use treated water for domestic purposes or animal consumption within the following period: 0.3 ppm - 7 DAT; 3.0 ppm - 14 DAT; and 5.0 ppm - 25 DAT.

[1] The formulations are expressed in lb endothall ae/gal.
[2] The maximum single and seasonal application rates are expressed in concentration of the endothall acid. The 30 ppm seasonal maximum rate is equivalent to 6 applications at the maximum single use rate.
[3] No holding time is required prior to use of treated water for irrigation of crops.
NS = not specified.

Conclusions. The submitted labels are adequate to evaluate the residue data relative to the proposed use of endothall on irrigation canals.

860.1300: Nature of the Residue - Plants

DP# D321179, D. Soderberg, 8/30/2005

The nature of endothall residues in plants is adequately understood based on the acceptable alfalfa, cotton, and sugar beet metabolism studies reflecting use of the dipotassium salt of [^{14}C]endothall. An adequate cotton metabolism study is also available reflecting use of the mono-N,N-dimethylalkylamine salt of [^{14}C]endothall. HED has concluded that the metabolism studies using the dipotassium salt will also fulfill metabolism data requirements for the monoalkylamine salt as the two salts would be expected to behave similarly in plants. The HED Metabolism Committee (S. Funk, 11/8/96) has also concluded that the residues of concern for both risk assessment and tolerance enforcement in plant commodities include parent endothall and its monomethyl ester.

860.1300: Nature of the Residue - Livestock

DP# D321179, D. Soderberg, 8/30/2005

The qualitative nature of the endothall residues in livestock is adequately understood based on the acceptable poultry and goat metabolism studies. The HED Metabolism Committee has concluded that the residues of concern in animal commodities consist of parent endothall and its monomethyl ester.

860.1340 Residue Analytical Methods

DP# D321179, D. Soderberg, 8/30/2005

Enforcement Methods

An enforcement method (GC with microcoulometric nitrogen detection) is listed as Method I in the Pesticide Analytical Manual (PAM, Volume II) for the determination of endothall in plant commodities. Using this method, residues in crop commodities are extracted using acetone acidified with HCl. The extract is concentrated, and the oil and oil-soluble materials are removed by partitioning solvents. The endothall containing oil-free fraction is concentrated by boiling with acetic acid. Any endothall present is converted to the N-methoxyimide derivative by reaction with methoxyamine hydrochloride. The imide is partitioned into chloroform, concentrated and analyzed by GC using a nitrogen specific detector. The method LOQ is 0.1 ppm.

A confirmatory HPLC/MSD method (Method No. KP218R0) is also available for determining residues of endothall and its monomethyl ester in fish and residues of endothall in plant commodities. For this method, residues are extracted with water, acidified and, if necessary, purified using a C_{18} SPE column. Residues are then derivatized with heptafluoro-*p*-tolylhydrazine (HFTH) and partitioned into dichloromethane (DCM). Derivatized residue are concentrated, redissolved in toluene, and cleaned up using a silica gel cartridge. Residues are determined by HPLC/MSD using the 397 amu ion for detection and quantitation. The validated LOQ is 0.05 ppm for fish (endothall and endothall monomethyl ester), and the LOQs for plant commodities range from 0.01-0.10 ppm, with the initial C_{18} SPE cleanup step. This method has undergone a successful independent laboratory validation using fish samples.

Data Collection Methods

In the irrigated crop field trials and processing studies, residues of endothall in/on plant commodities were determined using a LC/MS/MS method (Method No. KP-242R1) entitled "Analytical Method for Determination of Endothall in Crops", issued 5/4/2007. For this method, residues are extracted from all matrices, except oil, by homogenization with water followed by centrifugation and filtering. For oil samples, the samples are initially diluted with water and partitioned against hexane, discarding the organic fraction. The aqueous soluble residues from all matrices are then derivatized with HFTH in 50% H_3PO_4 at 100-120°C for 90 minutes. The derivatized residues are partitioned into methyl t-butyl ether (MTBE), concentrated, and reconstituted in hexane:MTBE (1:1 v/v). Residues are then cleaned up using an amine SPE cartridge eluted with methanol:MTBE (4:1,v/v) or methanol. Residues are analyzed by LC/MS/MS using external standards, and the m/z 397→166 ion transition was used for quantifying residues. Residues are expressed in endothall acid equivalents. The validated LOQ is 0.05 ppm for plant commodities.

In conjunction with the irrigated crop field trials, the above method was adequately validated on all plant matrices tested.

Conclusions. Adequate methods are available for enforcing the proposed tolerances, and the residue data from the field trials and processing studies were collected using an adequate LC/MS/MS method. The conditions for the derivatization step used in Method No. KP-242R1 should hydrolyze the monomethyl ester to the free acid. However, no data were provided as to whether or not the LC/MS/MS method can recover residues of the methyl ester of endothall, which are also residues of concern.

860.1360 Multiresidue Methods

DP# D321179, D. Soderberg, 8/30/2005

Adequate data are available evaluating the recovery of endothall using the FDA multiresidue methods published in the FDA Pesticide Analytical Manual, Volume I (PAM Vol. I). The available data indicate that endothall is not recovered through the FDA multiresidue methods.

860.1380 Storage Stability

DP# D321179, D. Soderberg, 8/30/2005
47520719.der.doc

Adequate storage stability data are available indicating that endothall is stable under frozen storage conditions for up to 5.5 years in rice, broccoli, oranges and tomatoes; 15 months in sugar beet tops and roots; 12 months in potatoes and cottonseed; and 9 months in alfalfa seed.

Additional storage stability data were also submitted with the current petition. In this study, control samples of tomato, lettuce, sugar beet root, corn grain and soybean seeds and oil were fortified with endothall (free acid) and stored at ≤-8°C. Stored samples of frozen tomatoes, lettuce, sugar beet roots and corn grain were analyzed after 0, 1, 10 and 15 months of storage and the frozen soybean seed and oil samples were analyzed after 0, 1, 5 and 10 months of storage. Endothall residues were completely stable for up to 15 months in frozen tomatoes, lettuce, sugar beet roots, and corn grain and for up to 10 months in soybean seeds and oil. The tests on soybean seeds and oil are on-going.

The storage durations and conditions of samples from the irrigated crop field trials submitted to support this petition are presented in Table 4.

Table 4. Summary of Storage Conditions and Durations of Samples from Irrigated Crop Field Trial and Processing Studies.

Matrix	Storage Temperature (°C)	Actual Storage Duration (days)	Interval of Demonstrated Storage Stability (days)
Field Trials			
Carrot	≤-18	33-272	469
Potato		41-58	
Sugar beet tops and roots		47-64	
Onions, green and bulb	≤-18	63- 143	469
Lettuce	≤-18	34-92	469
Cabbage	≤-18	61-118	469
Lima beans, succulent podded	≤-10	93-431	315-469
Dried beans		63-76	
Garden peas, succulent podded		113-127	
Soybean seed		39-385	
Tomatoes	≤-11	77-106	~2000
Cucumbers	≤-10	478	~2000
Oranges	≤-18	105-107	~2000
Apples	≤-18	230	~2000
Peaches	≤-10	154	~2000
Blueberries and blackberries	≤-18	85-98	~2000
Pecan nutmeat	≤-18	203	315-469
Almond nutmeats and hulls		90-96	
Corn, K+CWHR, forage, grain, and stover	≤-10	42-238	466-469
Sorghum forage, grain and stover	≤-10	51-83	466-469
Wheat forage, grain, hay and straw	≤-10	42-113	466-469
Grass forage and hay	≤-10	404-440	469
Alfalfa Forage and hay	≤-18	66-83	469
Grapes	≤-10	88-379	467
Mint tops	≤-18	22-336	469
Rice grain and straw	≤-10	64-99	466-469
Processing Studies			
Sugar beet roots, dried pulp, molasses and refined sugar	≤-18	19-64	465
Soybean seed, hulls, meal and refined oil	≤-10	17-78	306-315
Tomato fruit, paste and puree	≤-5	77-80	~2000
Orange fruit, dried pulp, juice and oil	≤-18	109-121	~2000 306 (oil)

Table 4. Summary of Storage Conditions and Durations of Samples from Irrigated Crop Field Trial and Processing Studies.

Matrix	Storage Temperature (°C)	Actual Storage Duration (days)	Interval of Demonstrated Storage Stability (days)
Apple fruit, juice and wet pomace	≤-18	231-286	~2000
Sorghum grain and flour	≤-10	26	~2000
Wheat grain, middlings, bran, flour, shouts and germ	≤-10	34-79	~2000
Corn grain, grits, meal, flour, starch, and oil	≤-10	22-37	~2000 306 (oil)
Grape fruit, juice and raisins	≤-10	377-379	~2000
Mint Tops	≤-17	22-336	467
Mint Oil		241	306
Rice grain, hulls, bran and polished rice	≤-10	39-48	~2000

Conclusions. The available storage stability data are adequate and support the sample storage conditions and durations from the irrigated crop field trials.

860.1400 Water, Fish, and Irrigated Crops

Fish.

DP# D307060 D. Soderberg 8/23/2004

Residue data were submitted (MRIDs 44820102, 43315801 and 42644001) showing metabolism of endothall in fish, bioconcentration of endothall residues in fish, and magnitude of the residue data in fish. Most of the endothall radioactive residue was incorporated into natural components of the fish. No endothall, per se, or either of its methyl esters were identified in the metabolism study, but one could infer from the combination of studies and other correlate information, that the residues of interest would be endothall and its monomethyl and dimethyl esters.

A magnitude of the residue study was performed using bluegill, catfish, crayfish, and freshwater clams in seven treated fresh water tanks and one control tank. Using a method with an LOQ of 0.02 ppm, residues of endothall, per se, were not detected in catfish, were up to 0.026 ppm in bluegills, up to 0.23 ppm in crayfish and in freshwater clams were up to 0.96 ppm. There was no measurable contribution to the residue from either of the methyl esters, however recovery of the methyl esters was not good.

Consistent with the registrant's proposal for tolerance, HED agreed that these data could support tolerances at 0.1 ppm for fish, 1 ppm for crustaceans, and 4 ppm for mussels - pending submission of either a revised metabolism study or a radio-validation study more clearly showing the importance of the methyl esters in the total residue, or revised residue data using a method showing better recovery of the two methyl esters. A tolerance of 0.1 ppm has since been published for fish.

Irrigated Crops.

DP# D321179, D. Soderberg, 8/30/2005

47520701.del.doc	(Sugar beet, carrot, potato)	47520702.der.doc	(Green and dry bulb onions)
47520703.der.doc	(Cabbage)	47520704.der.doc	(Leaf and head lettuce)
47520705.del.doc	(Legume vegetables)	47520706.del.doc	(Tomato)
47520707.der.doc	(Cucumber)	47520708.del.doc	(Orange)
47520709.del.doc	(Apple)	47520710.def.doc	(Peach)
47520711.der.doc	(Blueberry and blackberry)	47520712.der.doc	(Pecan and Almond)
47520713.del.doc	(Corn, sorghum and wheat)	47520714.der.doc	(Grass)
47520715.der.doc	(Alfalfa)	47520716.del.doc	(Grape)
47520717.del.doc	(Mint)	47520718.del.doc	(Rice)

Residue data supporting the use of endothall-treated water for irrigation of crops were previously submitted on cabbage, celery, grapefruits, peppers, and turnips as representative crops (DP# D321179, D. Soderberg, 8/30/2005). In these earlier tests, the SC/L or G formulations of the monoalkylamine or dipotassium salts for endothall were applied to the above crops at a concentration of ~3 ppm using overhead or furrow irrigation, with each crop receiving 5-7 applications. HED concluded that these data were not adequate because endothall was not applied at the maximum use rate allowed for irrigation canals (5 ppm) and because the data were insufficient to cover all irrigation crops.

In response, IR-4 submitted a protocol for conducting limited field trials on representative irrigated crops. This protocol was discussed with ChemSAC, which provided only minor comments (ChemSAC minutes for 5/12/06 meeting). Subsequently, IR-4 has submitted limited field trial data covering a wide variety of crops and crop groups that could be irrigated with endothall-treated water, including: carrots, potatoes and sugar beets (groups 1 and 2); green and dry bulb onions (group 3); leaf and head lettuce (group 4); cabbage (group 5); dried and succulent (podded) peas and beans (group 6); tomatoes (group 8), cucumbers (group 9); oranges (group 10), apples (group 11), peaches (group 12), blueberries and blackberries (group 13); almonds and pecans (group 14); corn, sorghum, wheat and rice (groups 15 and 16); grass (group 17); alfalfa (group 18); and mint. Although the field trials cover a wide variety of crops, the number of field trials conducted on any given crops was limited, ranging from 2 to 4 tests per crop.

In each field trial, the monoalkylamine salt of endothall (2 lb ae/gal SC/L) was used to treat the irrigation water at a rate of ~5 ppm ae (ae), and the treated water was then applied via overhead sprinklers as six broadcast foliar applications at RTIs of ~7 days. The target application volume in each trial was equivalent to ~1 acre inch of water (27,154 gal/A). Based on the concentration of the endothall in the irrigation water and the amount of water applied, the target application rate for endothall was equivalent to 1.13 lb ae/A/application, for a total of 6.79 lb ae/A/season. Side-by-side tests were also conducted on selected crop (sugar beets, lettuce, cucumber, and peaches) comparing application of the dipotassium salt of endothall (3 lb ae/gal SC/L) with the monoalkylamine salt. However, although the dipotassium salt was applied to the irrigation water according to the label directions for that salt, the resulting concentration of endothall in the water was 3.5 ppm ae. [Unlike the label directions for the alkylamine salt, the label directions for the potassium salt assume that it is applied at 5 ppm as the salt, not as the acid equivalent, that is to say, the potassium salt labeled instructions describe application at 5 ppm ai, not 5 ppm ae.]

In each field trial, the endothall residues were determined using an adequate LC/MS/MS method (Method No. KP-242R1), which is described in the above Residue Analytical Methods Section. The method was validated in conjunction with each trial, and the validated LOQ for endothall is 0.05 ppm in each commodity. The sample storage conditions and durations for the various crop commodities from each of the field trials are supported by the available storage stability data. The details for each of the submitted field trials are discussed below, and the endothall residues in the commodities are summarized in Table 5.

TABLE 5. Summary of Residue Data from Field Trials with Endothall.										
Commodity	Formulation type	Total Applic. Rate [1]	PHI (days)	Residue Levels (ppm) [2]						
				n	Min.	Max.	HAFT [3]	Median (STMdR)	Mean (STMR)	Std. Dev.
Root and Tuber Vegetables										
Sugar beet, tops	Monoamine salt (SC/L)	5 ppm (6.77-6.79)	0	2	1.32	1.36	1.36	1.34	1.34	0.033
	Dipotassium salt (SC/L)	3.5 ppm (4.80-4.88)	0	2	0.527	1.114	1.114	0.820	0.820	0..415
Sugar beet, roots	Monoamine salt (SC/L)	5 ppm (6.77-6.79)	0	2	0.165	0.493	0.493	0.330	0.330	0.230
	Dipotassium salt (SC/L)	3.5 ppm (4.80-4.88)	0	2	0.118	0.330	0.331	0.224	0.224	0.151
Carrot	Monoamine salt (SC/L)	5 ppm (6.77-6.79)	0	2	0.0685	0.088	0.088	0.078	0.078	0.014
Potato	Monoamine salt (SC/L)	5 ppm (6.77-6.83)	0	2	0.0725	0.875	0.0875	0.080	0.080	0.011
Bulb Vegetables										
Green Onion	5.0 ppm (6.75)		0	1	0.259	0.259	0.259	0.259	0.259	NA
Dry Bulb onion	5.0 (6.76)		0	1	<0.05	<0.05	<0.05	<0.05	<0.05	NA
Leafy Green Vegetables – Lettuce										
Leaf lettuce	Monoamine salt (SC/L)	5 ppm (6.73-6.76)	0	2	0.436	.9915	0.9915	0.714	0.714	0.393
	Dipotassium salt (SC/L)	3.5 ppm (4.67-4.81)	0	2	0.248	0.7975	0.7975	0.523	0.523	0.363
Head lettuce	Monoamine salt (SC/L)	5 ppm (6.76-7.17)	0	2	0.0865	0.5475	0.5475	0.292	0.317	0.270
	Dipotassium salt (SC/L)	3.5 ppm (4.81-5.07)	0	2	0.066	0.509	0.509	0.2875	0.2875	0.3132
Brassica - Cabbage										
Cabbage, head with wrapper leaves	5 ppm (5.64-7.00)		0	2	0.0615	0.0625	0.0625	0.062	0.062	0.0007
Legume Vegetables										
Succulent podded beans	5 ppm (6.75, 9.02) [4]		0	2	0.3075	0.4675	0.4675	0.3875	0.3875	0.113
Succulent podded peas	5 ppm (6.74)		0	2	0.5295	0.939	0.939	0.734	0.734	0.290
Dried Beans	5 ppm (6.77)		0	2	0.102	0.116	0.116	0.109	0.109	0.010
Soybean, dried seed	5 ppm (6.75-6.77)		0-1	4	<0.050	0.07	0.07	0.034	0.034	0.025

TABLE 5. Summary of Residue Data from Field Trials with Endothall.										
Commodity	Formulation type	Total Applic. Rate [1]	PHI (days)	Residue Levels (ppm) [2]						
				n	Min.	Max.	HAFT [3]	Median (STMdR)	Mean (STMR)	Std. Dev.
Fruiting Vegetables – Tomatoes										
Tomato	5 ppm (6.74-6.77)		0	2	<0.05	<0.05	<0.05	0.05	0.05	N/A
Cucurbits - Cucumbers										
Fruit	Monoamine salt (SC/L)	5 ppm (6.75-6.77)	0	2	0.259	0.738	0.738	0.499	0.499	0.339
Fruit	Dipotassium salt (SC/L)	3.5 ppm (4.80-4.81)	0	2	0.324	0.433	0.433	0.522	0.522	0.389
Citrus - Orange										
Orange	5 ppm (6.63-6.78)		0	2	0.0215	0.026	0.026	0.024	0.024	0.0032
Pome Fruit – Apple										
Apple	5 ppm (6.64-6.79)		0	2	0.039	0.043	0.043	0.041	0.041	0.0028
Stone Fruits – Peach										
Fruit	Monoamine salt (SC/L)	5 ppm (6.78-7.08)	0	2	0.044	0.152	0.152	0.098	0.098	0.076
Fruit	Dipotassium salt (SC/L)	3.5 ppm (4.82-5.05)	0	2	0.045	0.127	0.127	0.086	0.086	0.058
Berries										
Blueberry	5.0 ppm (6.77)		0	1	0.177	0.177	0.177	0.177	0.177	N/A
Blackberry	5.0 ppm (6.73)		0	1	0.328	0.328	0.328	0.328	0.328	N/A

TABLE 5. Summary of Residue Data from Field Trials with Endothall.										
Commodity	Formulation type	Total Applic. Rate [1]	PHI (days)	Residue Levels (ppm) [2]						
				n	Min.	Max.	HAFT [3]	Median (STMdR)	Mean (STMR)	Std. Dev.
Tree Nuts										
Pecan, nutmeat	5 ppm (7.01)		0	1	0.24	024	0.024	0.024	0.024	N/A
Almond, nutmeat	5 ppm (6.80)		0	1	0.037	0.037	<0.037	0.037	0.037	N/A
Almond, hulls			0	1	7.56	7.56	7.56	7.56	7.56	N/A
Cereals, except Rice										
Sweet Corn										
K+CWHR	5 ppm (6.75-6.91)		0	2	0.05	0.17	0.17	0.11	0.11	0.085
Forage w/o ears			0	2	0.585	1.23	1.23	0.908	0.908	0.456
Forage w/ears			0	2	0.445	0.97	0.97	0.708	0.708	0.371
Stover w/ears			0	2	0.635	4.88	4.88	2.758	2.758	3.002
Field Corn										
Forage	5 ppm (2.26-3.38) [5]		0	4	0.285	0.385	0.385	0.334	0.334	0.041
Grain	5 ppm (6.75-7.10)		0	4	0.04	0.05	0.05	0.05	0.05	0.005
Stover			0	4	1.44	3.19	3.19	2.08	2.08	0.82
Sorghum										
Forage	5 ppm (2.26-3.38) [5]		0	3	0.35	2.67	2.67	1.262	1.262	1.237
Grain	5 ppm (6.77)		0	3	0.645	1.21	1.21	1.00	1.00	0.311
Stover			0	3	0.96	4.90	4.90	2.91	2.91	1.97
Wheat										
Forage	5 ppm (2.19-3.39) [5]		0	4	0.685	2.13	2.13	1.15	1.15	0.662
Hay			0	4	1.055	3.09	3.09	1.94	1.94	0.89
Grain	5 ppm (6.58-6.77)		0-1	4	0.32	1.91	1.91	0.71	0.71	0.800
Straw			0-1	4	1.07	2.74	2.74	1.83	1.83	0.74
AGF				1	20.3	20.3	20.3	20.3	20.3	N/A
Grasses										
Forage	5 ppm (6.64-7.02)		0-2	6	1.94	2.73	2.73	2.21	2.21	0.32
Hay			0-2	6	5.87	13.65	13.65	8.77	8.77	3.00
Alfalfa										
Forage	5 ppm (5.94-6.58)		0	2	1.77	2.12	2.12	1.95	1.95	0.25
Hay			0	2	4.93	5.20	5.20	5.07	5.07	0.19
Grapes										
Grape	5.0 ppm (6.64-6.76)		0	3	0.405	0.642	0.642	0.522	0.522	0.119
Mint										
Mint	5 ppm (6.64-6.77)		0	2	1.49	2.80	2.80	2.14	2.14	0.923

TABLE 5. Summary of Residue Data from Field Trials with Endothall.										
Commodity	Formulation type	Total Applic. Rate [1]	PHI (days)	Residue Levels (ppm) [2]						
				n	Min.	Max.	HAFT [3]	Median (STMdR)	Mean (STMR)	Std. Dev.
Rice										
Rice grain	5 ppm (6.75-6.77)		0-1	4	0.756	1.18	1.18	1.05	1.05	0.200
Rice Straw			0-1	4	1.02	2.6	2.6	1.90	1.90	0.66

1 The endothall concentrations are expressed in acid equivalents, and the values in parentheses are the total application rates in terms of lb ae/A.
2 Residues are expressed in terms of the free acid. The LOQ is 0.05 ppm. The LOQ was used for all values reported as ≤LOQ.
3 HAFT = Highest Average Field Trial.
4 One of the succulent podded bean field trials used 8 applications rather than 6 applications due to slow plant growth and maturation.
5 Field corn forage, sorghum forage, and wheat forage and hay were harvested after only two or three applications.

Root and Tuber Vegetables (Group 1).

Two field trials each were conducted on sugar beets, carrots, and potatoes in Zones 5, 10 and 11 during 2006-2007. In each test, the monoalkylamine salt formulation of endothall (2 lb ae/gal SC/L) was used to treat the irrigation water at a rate of 5 ppm ae. In addition, in the two sugar beet field trials, side-by-side test were also conducted using the dipotassium salt of endothall applied to the irrigation water at a concentration of 3.5 ppm ae. The treated water was applied during vegetative development as six broadcast foliar applications using overhead sprinklers, at RTIs of 6-8 days. Based on the concentration of the endothall and the amount of water applied, the application rates for the monoalkylamine salt of endothall were equivalent to 1.13-1.14 lb ae/A/application, for a total of 6.77-6.83 lb ae/A/season. The application rates for the dipotassium salt were equivalent to 0.80-0.81 lb ae/A/application, for a total of 4.80-4.88 lb ae/A/season. Single control and duplicate treated samples of sugar beet roots and tops, carrot roots and potato tubers were harvested from the respective tests on the day of the final application (0 DAT).

Following six endothall (monoalkylamine salt) applications totaling 6.77-6.83 lb ae/A/season, endothall residues at 0 DAT were 1.11-1.62 ppm in/on 4 samples of sugar beet tops from 2 plots, 0.136-0.591 ppm in/on 4 samples of sugar beet roots from 2 plots, 0.062-0.088 ppm in/on 4 samples of carrot roots from 2 plots , and 0.067-0.103 ppm in/on 4 samples of potato tubers from 2 plots. Average endothall residues were 1.34 ppm for sugar beet tops, 0.330 ppm for sugar beet roots, 0.078 ppm for carrot roots, and 0.080 ppm for potato tubers. The HAFT residues were 1.36 ppm for sugar beet tops, 0.493 ppm for sugar beet roots and 0.088 ppm for both carrot roots and potato tubers. No residue decline data were provided. No phytotoxicity was reported in any of the tests.

Following six endothall (dipotassium salt) applications totaling 4.80-4.88 lb ae/A/season, endothall residues at 0 DAT were 0.523-1.28 ppm in/on 4 samples of sugar beet tops from 2 plots and 0.115-0.345 ppm in/on 4 samples of sugar beet roots from 2 plots. Average endothall residues were 0.821 ppm in/on sugar beet tops and 0.224 ppm in/on sugar beet roots, and HAFT residues in/on sugar beet tops and roots were 1.11 and 0.331 ppm, respectively. Average endothall residues in/on sugar beet tops and roots were 0.6x-0.7x lower for the dipotassium salt formulation than for the monoalkylamine salt formulation. The lower level of endothall residues for the dipotassium salt correlated closely with the lower use rate (0.7x) for the dipotassium salt.

Bulb Vegetables (Group 3).

In one green onion and one dry bulb onion field trial conducted during 2007 in Zones 6 and 10, respectively, the monoalkylamine salt formulation of endothall (2 lb ae/gal SC/L) was used to treat the irrigation water at a rate of 5 ppm ae. The treated water was applied to onions during vegetative development as six broadcast foliar applications using overhead sprinklers, at RTIs of 7-8 days. Based on the concentration of the endothall and the amount of water applied, the application rates for endothall were equivalent to 1.12-1.13 lb ae/A/application, for a total of 6.75-6.76 lb ae/A/season. Single control and duplicate treated samples of green onions and dry bulb onions were harvested from the respective tests on the day of the final application (0 DAT). Endothall residues at 0 DAT were 0.234 and 0.284 ppm in/on 2 samples from one plot of green onions and <0.05 ppm in/on 2 samples from one plot of dry bulb onions. The average residues were 0.259 ppm for green onions and <0.05 ppm for dry bulb onions. No residue decline data was provided, and no phytotoxicity was reported on the treated onion crops.

Leafy Vegetables, except Brassica (Group 4).

Two leaf lettuce field trials and two head lettuce field trials were conducted in Zones 1 and 10 during 2006-2007. Side-by-side tests were conducted in each field trial using irrigation water treated with either the monoalkylamine salt of endothall (2 lb ae/gal SC/L) at a concentration of 5 ppm ae, or the dipotassium salt of endothall (3.0 lb ae/gal SC/L) at a concentration of 3.5 ppm ae. The treated water was applied in each test during vegetative development as six broadcast foliar applications using overhead sprinklers, at RTIs of 6-8 days. Based on the endothall concentrations and the amount of water applied, the application rates for the monoalkylamine salt of endothall were equivalent to 1.12-1.20 lb ae/A/application, for a total of 6.73-7.17 lb ae/A/season. The application rates for the dipotassium salt were equivalent to 0.78-0.84 lb ae/A/application, for a total of 4.67-5.07 lb ae/A/season. Single control and duplicate treated samples of leaf lettuce and head lettuce (with wrapper leaves) were harvested from the respective tests on the day of the final application (0 DAT).

Following applications of the monoalkylamine salt at level equivalent to 6.73-7.17 lb ae/A/season, endothall residues at 0 DAT were 0.410-1.24 ppm in/on 4 samples of leaf lettuce from 2 plots and 0.081-0.604 ppm in/on 4 samples of head lettuce from 2 plots. Average endothall residues were 0.714 ppm for leaf lettuce and 0.317 ppm for head lettuce. The HAFT residues in/on leaf and head lettuce were 0.992 and 0.548 ppm, respectively. No phytotoxicity was reported on the treated lettuce.

Following six applications of the dipotassium salt at levels equivalent to 4.67-5.07 lb ae/A/season, endothall residues at 0 DAT were 0.241-1.01 ppm in/on 4 samples of leaf lettuce from 2 plots and <0.05-0.582 ppm in/on 4 samples of head lettuce from 2 plots. Average endothall residues were 0.523 ppm in/on leaf lettuce and 0.288 ppm in/on head lettuce, and HAFT residues in/on leaf and head lettuce were 0.798 and 0.509 ppm, respectively. Average endothall residues were lower (0.7x-0.9x) for the dipotassium salt than the monoalkylamine salt, which is comparable to the lower use rate for the dipotassium salt (0.7x).

Brassica Vegetables (Group 5).

In two cabbage field trials conducted during 2006 in Zone 1, the monoalkylamine salt formulation of endothall (2 lb ae/gal SC/L) was used to treat the irrigation water at a rate of 5 ppm ae. The treated water was applied to cabbage during vegetative development as six broadcast foliar applications using overhead sprinklers, at RTIs of 6-9 days. Based on the concentration of the endothall and the actual amount of water applied, the application rates for endothall were equivalent to 0.94 or 1.17 lb ae/A/application, for a total of 5.64 or 7.00 lb ae/A/season. Single control and duplicate treated samples of cabbages (with wrapper leaves) were harvested from each test on the day of the final application (0 DAT). Endothall residues at 0 DAT were <0.05-0.075 ppm in/on 4 samples of cabbage from 2 plots. The average residues were 0.062 ppm and the HAFT residues were 0.063 ppm. No residue decline data were provided, and no phytotoxicity was noted on the treated cabbage.

Legume Vegetables (Group 6).

A total of 10 tests were conducted on legume vegetables in Zones 1, 4, 5, 10 and 12 during 2006-2007, including 2 tests on succulent podded beans, 2 tests on dry beans, 2 tests on succulent podded peas, and 4 tests on soybeans. In each test, a monoalkylamine salt formulation of endothall (2 lb ae/gal SC/L) was used to treat the irrigation water at a rate of 5 ppm ae. The treated water was applied during flowering through pod and seed development as broadcast foliar applications using overhead sprinklers, at RTIs of 6-9 days. A total of six applications were made in each test, except in one of the succulent bean tests, which used eight applications. Based on the concentration of the endothall and the amount of water applied, the application rates for endothall were equivalent to 1.12-1.13 lb ae/A/application, for a total of 6.74-6.77 lb ae/A for the six applications or 9.02 lb ai/A for the eight applications. Single control and duplicate treated samples of legume pods with seeds were harvested from the succulent bean and pea field trials and samples of dried seeds were harvested from the dry bean and soybean field trials.

Endothall residues were 0.291-0.521 ppm in/on 4 samples of succulent podded beans from 2 plots, 0.522-1.00 ppm in/on 4 samples of succulent podded peas from 2 plots, 0.070-0.134 ppm in/on 4 samples of dried beans from 2 plots, and <0.05-0.072 ppm in/on 8 samples of soybeans from 4 plots harvested at 0-1 DAT. Average endothall residues were 0.388 ppm for succulent podded beans, 0.734 ppm for succulent podded peas, 0.109 ppm for dry beans, and 0.055 ppm for soybeans. The HAFT residues were 0.468 ppm for succulent podded beans, 0.939 ppm for succulent podded peas, 0.116 ppm for dry beans, and 0.070 ppm for soybeans. No residue decline data was provided. Phytotoxicity was reported on plants at two field site, and consisted of chlorosis and necrosis of leaves.

Fruiting Vegetables, except cucurbits (Group 8).

In two tomato field trials conducted during 2006 in Zones 3 and 10, a monoalkylamine salt formulation of endothall (2 lb ae/gal SC/L) was used to treat the irrigation water at a rate of 5 ppm ae. The treated water was applied to tomatoes during flowering and fruit development as six broadcast foliar applications using overhead sprinklers, at RTIs of 6-8 days. Based on the concentration of the endothall and the amount of water applied, the application rates for endothall were equivalent to 1.12-1.13 lb ae/A/application, for a total of 6.74-6.77 lb ae/A/season. Single control and duplicate treated samples of tomatoes were harvested from each test on the day of the final application (0 DAT). Endothall residues at 0 DAT were <0.05 ppm in/on 4 samples of tomatoes from 2 plots. No residue decline data were provided, and no phytotoxicity was reported on the treated tomato crops.

Cucurbit Vegetables (Group 9).

Two cucumber field trials were conducted in Zones 1 and 5 during 2006-2007. In each trial, side-by-side tests were conducted using irrigation water treated with either the monoalkylamine salt of endothall (2 lb ae/gal SC/L) at a concentration of 5 ppm ae, or the dipotassium salt of endothall (3 lb ae/gal SC/L) at a concentration of 3.5 ppm ae. The treated water was applied in each test during flowering and fruit development as six broadcast foliar applications using overhead sprinklers, at RTIs of 6-8 days. Based on the endothall concentration and the amount of water applied, the application rate for the monoalkylamine salt of endothall was equivalent to 1.13 lb ae/A/application, for a total of 6.75-6.77 lb ae/A/season. The application rate for the dipotassium salt was equivalent to 0.80 lb ae/A/application, for a total of 4.80-4.81 lb ae/A/season. Single control and duplicate treated samples of cucumber were harvested from each test on the day of the final application (0 DAT).

Endothall residues were 0.234-0.738 ppm in/on 4 cucumber samples from 2 plots harvested at 0 DAT following irrigation applications of the monoalkylamine salt of endothall at 5 ppm ae, and were 0.310-0.459 ppm in/on 4 cucumber samples from 2 plots harvested at 0 DAT following six irrigation applications of the dipotassium salt of endothall at 3.5 ppm. Average endothall residues in/on cucumbers were 0.499 and 0.522 ppm for the monoalkylamine and dipotassium salt formulations, respectively. The HAFT residues were 0.738 and 0.433 ppm for the monoalkylamine and dipotassium salt formulations, respectively. Average endothall residues were lower (0.8x) for the dipotassium salt than the monoalkylamine salt, which was comparable to the lower use rate for the dipotassium salt (0.7x).

Phytotoxicity was reported in one of the tests, and consisted of the loss of older leaves, stunting of growing tips, cupping of young leaves, chlorosis, and cessation of flowering. However, fruit set and growth were not effected.

Citrus Fruits (Group 10).

In two orange field trials conducted during 2006 in Zones 3 and 10, a monoalkylamine salt formulation of endothall (2 lb ae/gal SC/L) was used to treat the irrigation water at a rate of 5 ppm ae. The treated water was applied to the orange trees during fruit development as six broadcast foliar applications using overhead sprinklers, at RTIs of 5-8 days. Based on the concentration of the endothall and the amount of water applied, the application rates for endothall were equivalent to 1.10-1.13 lb ae/A/application, for a total of 6.63-6.78 lb ae/A/season. Single control and duplicate treated samples of oranges were harvested from each test on the day of the final application (0 DAT). Endothall residues were <LLMV in/on 4 orange samples from 2 plots at 0 DAT, with residues above the LOD on all four samples at 0.021-0.028 ppm. The average and HAFT residues were 0.024 ppm and 0.026 ppm, respectively, in/on oranges. No phytotoxicity was reported on the treated trees.

Pome Fruits (Group 11).

In two apple field trials conducted during 2006 in Zones 1 and 11, a monoalkylamine salt formulation of endothall (2 lb ae/gal SC/L) was used to treat the irrigation water at a rate of 5 ppm ae. The treated water was applied to the apple trees during fruit development as six broadcast foliar applications using overhead sprinklers, at RTIs of 7 days. Based on the concentration of the endothall and the amount of water applied, the application rates for endothall were equivalent to 1.11-1.13 lb ae/A/application, for a total of 6.64-6.79 lb ae/A/season. Single control and duplicate treated samples of apples were harvested from each test on the day of the final application (0 DAT). Endothall residues at 0 DAT were <LLMV in/on 4 samples of apples from 2 plots, but were greater than the LOD, at 0.031-0.047 ppm, in 3 of the 4 samples. The average and HAFT residues were 0.041 ppm and 0.043 in/on apples. Phytotoxicity was noted on the treated trees (necrotic spots on leaves), but no damage was noted on the fruits.

Stone Fruits (Group 12).

Two peach field trials were conducted in Zones 2 and 10 during 2007. In each trial, side-by-side tests were conducted using irrigation water treated with either the monoalkylamine salt of endothall (2 lb ae/gal SC/L) at a concentration of 5 ppm ae, or the dipotassium salt of endothall (3 lb ae/gal SC/L) at a concentration of 3.5 ppm ae. The treated water was applied in each test during fruit development as six broadcast foliar applications using overhead sprinklers, at RTIs of 6-8 days. Based on the endothall concentration and the amount of water applied, the application rate for the monoalkylamine salt of endothall was equivalent to 1.13-1.25 lb ae/A/application, for a total of 6.78-7.08 lb ae/A/season. The application rate for the dipotassium salt was equivalent to 0.79-0.91 lb ae/A/application, for a total of 4.82-5.05 lb ae/A/season. Single control and duplicate treated samples of peaches were harvested from each test on the day of the final application (0 DAT).

Endothall residues at 0 DAT in/on peaches were <0.05-0.160 ppm in/on 4 samples from 2 plots treated with the monoalkylamine salt and <0.05-0.136 ppm in/on the 4 samples from 2 plots treated with dipotassium salt. Average endothall residues in/on peaches were 0.098 and 0.086 ppm for the monoalkylamine and dipotassium salt formulations, respectively. The HAFT residues were 0.152 and 0.127 ppm for the monoalkylamine and dipotassium salt formulations, respectively. Average endothall residues were lower (0.9x) for the dipotassium salt than the monoalkylamine salt, which is comparable to the lower use rate for the dipotassium salt (0.7x). Phytotoxicity was reported on the treated peach trees.

Berries (Group 13).

In one blueberry and one blackberry field trial conducted during 2007 in Zones 5 and 11, respectively, a monoalkylamine salt formulation of endothall (2 lb ae/gal SC/L) was used to treat the irrigation water at a rate of 5 ppm ae. The treated water was applied to the berry crops during fruit development and maturation as six broadcast foliar applications using overhead sprinklers, at RTIs of 6-8 days. Based on the concentration of the endothall and the amount of water applied, the application rates for endothall were equivalent to 1.12-1.13 lb ae/A/application, for a total of 6.73-6.77 lb ae/A/season. Single control and duplicate treated samples of blueberries and blackberries were harvested from the respective tests on the day of the final application (0 DAT).

Endothall residues at 0 DAT were 0.158 and 0.197 ppm in/on 2 samples of blueberry from 1 plot and 0.311 and 0.346 ppm in/on 2 samples of blackberry from 1 plot. The average residues were 0.177 and 0.328 ppm for blueberries and blackberries, respectively. No residue decline data was provided, and no phytotoxicity was reported on the treated crops.

Grapes.

In three grape field trials conducted in Zones 1, 10 and 11 during 2006 and 2007, a monoalkylamine salt of endothall (2 lb ae/gal SC/L) was used to treat the irrigation water at a rate of 5 ppm ae. The treated water was then applied using overhead sprinklers to the grapes as six broadcast foliar applications during fruit development at RTIs of 6-8 days. Based on the concentration of the endothall and the amount of water applied, the application rates for endothall were equivalent to 1.11-1.13 lb ae/A/application, for a total of 6.64-6.76 lb ae/A/season. Single control and duplicate treated samples of grapes were harvested on the day of the final application (0 DAT). Endothall residues in/on grapes harvested at 0 DAT were 0.376-0.696 ppm. The average residues were 0.522 ppm and the HAFT residues were 0.642 ppm. No residue decline data was provided. At two of the three field sites, phytotoxicity was noted beginning with the second application and increased in severity with subsequent applications. The leaves initially showed signs of chlorosis and browning, with leaf necrosis occurring at later applications.

Tree Nuts (Group 14).

In a pecan and almond field trial conducted during 2006-2007 in Zones 2 and 10, respectively, a monoalkylamine salt formulation of endothall (2 lb ae/gal SC/L) was used to treat the irrigation water at a rate of 5 ppm ae. The treated water was applied to the tree nut crops during nut development and maturation as six broadcast foliar applications using overhead sprinklers, at RTIs of 7-8 days. Based on the concentration of the endothall and the amount of water applied, the application rates for endothall were equivalent to 1.13-1.17 lb ae/A/application, for a total of 6.80-7.01 lb ae/A/season. Single control and duplicate treated samples of pecan and almond nutmeats and almond hulls were harvested from the respective tests on the day of the final application (0 DAT). No phytotoxicity was reported on the treated nut crops.

Endothall residues at 0 DAT were <LOQ in/on two samples each from 1 plot each of pecan and almond nutmeats. However, residues were detectable at 0.024 ppm in one of the pecan nutmeat samples and at 0.036 and 0.037 ppm in the two almond nutmeat samples. Residues in/on the two almond hull samples were 6.91 and 8.20 ppm. Average endothall residues and the HAFT residues were both 0.05 ppm for nutmeats and 7.56 ppm for almond hulls.

Cereal Grains (Except Rice).

A total of 13 field trials were conducted during 2006 and 2007 in Zones 1, 2, 5, 6, 7, and 11, including two trials on sweet corn, four trials on field corn, three trials on sorghum, and four trials on wheat (3 winter wheat and 1 spring wheat). In each test, the monoalkylamine salt formulation of endothall (2 lb ae/gal SC/L) was used to treat the irrigation water at a rate of 5 ppm ae. The treated water was applied to each crop during seed head formation and development as six broadcast foliar applications using overhead sprinklers, at RTIs of 6-9 days.

Based on the concentration of the endothall in the irrigation water and the amount of water applied, the overall application rates for endothall were equivalent to 1.10-1.25 lb ae/A/application, for a total of 6.58-7.10 lb ae/A/season. Because samples of field corn forage, sorghum forage, and wheat forage and hay were harvested after only 2 or 3 applications, the total application rates for these commodities was 2.19-3.39 lb ae/A.

Duplicate control and treated samples of each commodity were harvested from the respective tests. Samples of field corn forage, sorghum forage and wheat forage and hay were harvested 0 days after the second or third application (0 DAT). Samples of sweet corn forage, kennels plus cob with husks removed (K+CWHR) and stover, field corn grain and stover, sorghum grain and stover, and wheat grain and straw were harvested following the sixth application at 0 DAT (or at 1 DAT in one wheat test).

In the sweet corn field trials, endothall residues at 0 DAT were <0.05-0.17 ppm in/on 4 samples of K+CWHR, 0.52-1.28 ppm in/on 4 samples of forage without ears, 0.40-1.06 ppm in/on 4 samples of forage with ears, and 0.58-5.06 ppm in/on 4 samples of stover with ears. Average endothall residues were 0.11 ppm for K+CWHR, 0.91 ppm for forage without ears, 0.71 ppm for forage with ears, and 2.76 ppm for stover with ears. The HAFT residues were 0.17 ppm in/on K+CWHR, 1.23 ppm in/on forage without ears, 0.97 ppm in/on forage with ears, and 4.88 ppm in/on stover with ears.

In the field corn field trials, endothall residues at 0 DAT were 0.21-0.42 ppm in/on 8 samples of forage harvested after only 2 or 3 applications (2.26-3.38 lb ae/A). Following all six applications (6.75-7.10 lb ae/A), endothall residues at 0 DAT were <0.05 ppm in/on 8 samples of grain and 1.07-3.48 ppm in/on 8 samples of stover from 4 plots each. Average endothall residues were 0.33 ppm for forage, <0.05 ppm for grain, and 2.08 ppm for stover. The HAFT residues were 0.385 ppm in/on forage, <0.05 ppm in/on grain, and 3.19 ppm in/on stover.

In the sorghum field trials, endothall residues at 0 DAT were 0.29-3.05 ppm in/on 6 samples of forage harvested from 3 plots after only 2 or 3 applications (2.26-3.38 lb ae/A). Following all six applications (6.77 lb ae/A), endothall residues at 0 DAT were 0.49-1.41 ppm in/on 6 samples of grain and 0.81-7.19 ppm in/on 6 samples of stover. Average endothall residues were 1.26 ppm for forage, 1.00 ppm for grain, and 2.91 ppm for stover. The HAFT residues were 2.67 ppm in/on forage, 1.21 ppm in/on grain, and 4.90 ppm in/on stover.

In the wheat field trials, endothall residues at 0 DAT were 0.63-2.27 ppm in/on 8 samples of forage and 1.00-3.09 ppm in/on 8 samples of hay harvested from 4 plots after only 2 or 3 applications (2.19-3.39 lb ae/A). Following all six applications (6.58-6.77 lb ae/A), endothall residues at 0 or 1 DAT were 0.20-2.01 ppm in/on 8 samples of grain and 0.61-2.76 ppm in/on 8 samples of straw from 4 plots each. Average endothall residues were 1.15 ppm for forage, 1.94 ppm for hay, 0.71 ppm for grain, and 1.83 ppm for straw. The HAFT residues were 2.13 ppm in/on forage, 3.09 ppm in/on hay, 1.91 ppm in/on grain, and 2.74 ppm in/on straw. Residue decline data were not provided in any field trials, and no phytotoxicity was reported for any of the treated cereal grain crops.

Rice.

In four rice field trials conducted during 2007 in Zones 4, 6 and 10, a monoalkylamine salt formulation of endothall (2 lb ae/gal SC/L) was used to treat the irrigation water at a rate of 5 ppm ae. The treated water was applied to the rice during grain development and maturation as six broadcast foliar applications using overhead sprinklers, at RTIs of 6-8 days. Based on the concentration of the endothall and the amount of water applied, the application rates for endothall were equivalent to 1.13 lb ae/A/application, for a total of 6.75-6.77 lb ae/A/season. Single control and duplicate treated samples of rice grain and straw were harvested from each test on the day of the final application or one day later (0-1 DAT). Endothall residues were 0.69-1.22 ppm in/on 4 samples of rice grain and 0.94-2.61 ppm in/on 4 samples of rice straw harvested from 2 plots each at 0-1 DAT. Average endothall residues were 1.01 ppm for grain and 1.90 ppm for straw, and the HAFT residues were 1.18 ppm for grain and 2.60 ppm for straw. No residue decline data was provided, and no phytotoxicity was reported on the treated rice.

Grass forage and hay (Group 17).

A total of six grass field trials were conducted in Zones 4, 6, 11 and 12 during 2006 and 2007, including 2 field trials each on bluegrass, Bermuda grass, and fescue grass. In each test, the monoalkylamine salt formulation of endothall (2 lb ae/gal SC/L) was used to treat the irrigation water at a rate of 5 ppm ae. The treated water was applied to the grass during vegetative development as six broadcast foliar applications using overhead sprinklers, at RTIs of 6-10 days. Based on the concentration of the endothall in the irrigation water and the amount of water applied, the application rates for endothall were equivalent to 1.11-1.17 lb ae/A/application, for a total of 6.64-7.02 lb ae/A/season. Duplicate control and treated samples of grass forage and hay were harvested on either the day of the final application (0 DAT) in the fescue tests, at 1 DAT in the Bermuda grass tests, or at 1-2 DAT in the bluegrass tests. The forage samples were collected immediately after harvest, and the hay samples were field-dried for 2-6 days prior to collection.

Endothall residues were 1.70-2.86 ppm in/on 12 forage samples and 5.34-14.2 ppm in/on 12 hay samples harvested from 6 plots each at 0-2 DAT. Average endothall residues were 2.21 ppm for forage and 8.77 ppm for hay, and the HAFT residues were 2.73 ppm for forage and 13.65 ppm for hay. No residue decline data were provided. Phytotoxicity was reported on the treated bluegrass at one field site, and consisted of stunting and slight chlorosis

Nongrass Animal Feeds (Forage, Fodder and Hay) (Group 18).

In two alfalfa field trials conducted during 2007 in Zones 5 and 7, a monoalkylamine salt formulation of endothall (2 lb ae/gal SC/L) was used to treat the irrigation water at a rate of 5 ppm ae. The treated water was applied to the alfalfa during vegetative development as six broadcast foliar applications using overhead sprinklers, at RTIs of 6-8 days. Based on the concentration of the endothall in the irrigation water and the amount of water applied, the application rates for endothall were equivalent to 0.99-1.10 lb ae/A/application, for a total of 5.94-6.58 lb ae/A/season. Duplicate control and treated samples of alfalfa forage and hay were harvested from each test on the day of the final application (0 DAT), and the hay samples were field-dried for 1-5 days prior to collection.

Endothall residues were 1.41-2.24 ppm in/on 4 forage samples and 3.09-5.31 ppm in/on 4 hay samples harvested from 2 plots at 0 DAT. Average endothall residues were 1.95 ppm for forage and 5.07 ppm for hay, and the HAFT residues were 2.12 ppm for forage and 5.20 ppm for hay. No residue decline data were provided. No phytotoxicity on the treated alfalfa was reported at either test site.

Mint.

In two mint field trials conducted during 2006 and 2007 in Zones 5 and 11, a monoalkylamine salt formulation of endothall (2 lb ae/gal SC/L) was used to treat the irrigation water at a rate of 5 ppm ae. The treated water was applied to the mint during vegetative development as six broadcast foliar applications using overhead sprinklers, at RTIs of 6-7 days. Based on the concentration of the endothall and the amount of water applied, the application rates for endothall were equivalent to 1.11-1.13 lb ae/A/application, for a total of 6.64-6.77 lb ae/A/season. Single control and duplicate treated samples of mint tops were harvested from each test on the day of the final application (0 DAT). Endothall residues were 1.31-2.89 ppm in/on 4 samples of mint tops harvested from 2 plots at 0 DAT. Average endothall residues were 2.14 ppm, and the HAFT residues were 2.80 ppm. No residue decline data was provided. At one of the field sites, the treated mint exhibited signs of phytotoxicity, which consisted of reduced development and stunting of the crop.

Conclusions. Issues pertaining to residues in potable water and fish have been resolved and are discussed in the Residue Chemistry Chapter of the Endothall RED (DP# D321179, D. Soderberg, 8/30/2005).

The submitted field trial data on irrigated crops were conducted according the previously submitted protocol. Two to four field trials were conducted for each representative crop in the major growing regions for the respective crops. With only a couple of exceptions, sample of regulated commodities were harvested at 0 DAT from each field trial. Samples were analyzed for residues of endothall using an adequate LC/MS/MS method, and the sample storage durations and conditions are supported by the available storage stability data.

The submitted data are generally adequate for assessing inadvertent residues of endothall on irrigated crops. In addition, the residues determined in the 0 DAT samples will represent an over-estimate of residues for many of the crops tested, because, because application is at the maximum rate, is all applied by overhead irrigation, and irrigation on the day of harvest would be highly unlikely to occur due to commercial harvesting procedures. Crops and commodities which would be unlikely to be irrigated prior to harvest include: sugar beets, carrots, potatoes, dry bulb onions, dried peas and beans, soybeans, tree nuts, field corn grain and stover, sorghum grain and stover, wheat grain and straw, and rice grain and straw.

In addition, HED notes that phytotoxicity was reported on a number of the crops tested, including legume vegetables, cucumbers, apple trees, peach trees, grape vines, mint and grass. The phytotoxicity generally appeared beginning after the second application and consisted of leaf chlorosis and necrosis, with some crops also having reduced growth and stunting. The occurrence of phytotoxicity on a wide range of crops suggests that repeated irrigation with water containing high levels (5 ppm) endothall is unlikely to occur under normal agricultural condition.

Although the submitted data are deemed adequate for assessing tolerances for inadvertent residues on irrigated crops, the following deficiencies were noted in the submitted field trial data.

- The bridging studies comparing the use of the monoalkylamine and dipotassium salts of endothall were of limited use as the two formulations were applied at different rates. In terms of acid equivalents, the monoalkylamine salt was applied at a concentration of 5 ppm and the dipotassium salt was applied at a concentration of 3.5 ppm, which is the maximum allowed use rate of the dipotassium salt (0.7x rate for the monoalkylamine salt). For each of the crops tested with both salt formulations, endothall residues were 0.6-0.9x lower for the dipotassium salt than for the monoalkylamine salt, which is consistent with the lower use rate for the dipotassium salt. Although the bridging studies do not allow for direct comparison of the two salts, the data do indicate that endothall residues resulting from application of the dipotassium salt to irrigation canals will be lower than from the monoalkylamine salt, when both are applied according to current label directions.

- Spinach should have been used as the representative leafy vegetable crop, as foliar applications generally result in higher residues on spinach than on lettuce (leaf and head) or celery.

- Mustard greens should have been used as the representative Brassica vegetable crop, as foliar applications generally result in higher residues on mustard greens than on broccoli, cauliflower or cabbage.

- Field corn forage, sorghum forage and wheat forage and hay only received 2-3 applications prior to harvest. For these crops, separate plots should have been established for collection of forage and hay samples so that all six applications could have made prior to harvest of forage and hay.

- No field trials were conducted on an oil seed crop such as, canola, flax, safflower, or sunflower.

- No field trials were conducted on peanuts, which is a major field crop.

The levels of inadvertent residues for endothall supported by the available field trial data are listed in Table 10 and discussed below in the Proposed Tolerances Section.

860.1460 Food Handling

There are no registered uses that are relevant to this guideline topic.

860.1480 Meat, Milk, Poultry, and Eggs

DP# D321179, D. Soderberg, 8/30/2005

No cattle or poultry feeding studies are currently available for endothall, and the Endothall RED noted that these studies are required. Because IR-4 is proposing tolerances on a wide variety of livestock feedstuffs, the dietary burdens of livestock for endothall residues were recalculated for this petition based on the maximum reasonably balanced diets (MRBD). Using the proposed and recommended tolerances and the recent changes in calculating residues in MRBDs (Revisions of Table 1 Feedstuffs, June 2008), the MRBDs for livestock to endothall residues were calculated to be 8.97 ppm for beef cattle, 7.65 ppm for dairy cattle, 3.30 ppm for poultry and 3.58 ppm for swine (Table 6) based upon residues in the feeds.

In addition to the dietary exposure of livestock through the consumption of feedstuffs, the Endothall RED noted that livestock may also be exposed to endothall residues through the consumption of endothall-treated water. For purposes of setting tolerances it must be considered that livestock may be exposed to water at the maximum labeled value of 5 ppm. The potential contribution of endothall residues in water to the dietary exposure of livestock was calculated following the procedures described in PP#1F3991/1F3935 (G. Okatie, 9/4/92), based on the concentration of endothall in the drinking water, the daily water consumption, and the daily feed intake. The estimated values for daily water consumption and food intake (dry wt. basis) are presented in Table 7, along with the calculated contribution of the treated water to the dietary burden. When expressed on the basis of the dry feed intake, the contribution of endothall-treated water to the dietary burden would be 19.2 ppm for beef cattle, 45.4 ppm for dairy cattle, 13.5 ppm for poultry, and 16.1 ppm for swine. When combined with the exposure to endothall residues in feedstuffs, the total dietary exposure of livestock to endothall residues would be 27.7 ppm for beef cattle, 35.8 ppm for dairy cattle, 16.8 ppm for poultry, and 19.7 ppm for swine (as shown in Table 8.

Using the TRR estimated in the relevant livestock tissues after dosing in the metabolism it is possible to make some estimate of the maximum residues expected in the livestock tissues. In this way, residues in the tissues are estimated as shown in Table 9. However, given the levels of dietary exposure of livestock to endothall residues in both their feedstuffs and drinking water, cattle and poultry feeding studies are required and registration must be contingent upon submission of these studies.

Table 6. Calculation of Dietary Burdens of Endothall Residues in Livestock.

Feedstuff	Type[1]	% Dry Matter[2]	% Diet[2]	Recommended Tolerance (ppm)	Dietary Contribution (ppm)[3]
Beef Cattle R: 15%; CC: 80%; PC: 5%					
Grass, hay	R	88	15	18	3.07
Grain, aspirated fractions	CC	85	5	35	2.06
Wheat, milled byproducts	CC	88	40	5.0	2.28
Grain, cereal, group 15	CC	88	30	4.0	1.37
Sugar, beet, molasses	CC	75	5	1.5	0.1
Soybean, meal	PC	92	5	0.2[4]	0.01
TOTAL BURDEN			100		**8.9**
Dairy Cattle R: 45%; CC: 45%; PC: 10%					

Table 6. Calculation of Dietary Burdens of Endothall Residues in Livestock.					
Feedstuff	Type[1]	% Dry Matter[2]	% Diet[2]	Recommended Tolerance (ppm)	Dietary Contribution (ppm)[3]
Grass, hay	R	88	20	18	4.09
Almond, hulls	R	90	5	15	0.83
Animal feed, Nongrass, group 18, forage	R	35	20	4.0	2.29
Wheat, milled byproducts	CC	88	30	5.0	1.70
Grain, cereal, group 15	CC	88	10	4.0	0.46
Sugar, beet, molasses	CC	75	5	1.5	0.1
Soybean, meal	PC	92	10	0.2[4]	0.02
TOTAL BURDEN			100		9.5
Poultry CC: 75%; PC: 25%					
Grain, cereal, group 15	CC	88	75	4.0	3.0
Alfalfa , meal, (Animal feed, Nongrass, group 18, hay)	PC	89	5	10.0	0.5
Soybean, meal	PC	92	20	0.2[4]	0.04
TOTAL BURDEN	--	--	100	--	3.6
Swine CC: 85 %; PC: 15%					
Grain, cereal, group 15	CC	88	85	4.0	3.4
Alfalfa , meal, (Animal feed, Nongrass, group 18, hay)	PC	89	5	10.0	0.5
Soybean, meal	PC	92	10	0.2[4]	0.02
TOTAL BURDEN	--	--	100	--	4.0

[1] R: Roughage; CC: Carbohydrate concentrate; PC: Protein concentrate.
[2] OPPTS 860.1000 Table 1 Feedstuffs (June 2008).
[3] Contribution = ([tolerance /% DM] X % diet) for beef and dairy cattle; contribution = ([tolerance] X % diet) for poultry and swine.
[4] The tolerance for soybean seeds was used for soybean meal.

Table 7. Calculation of Dietary Burdens of Endothall Residues to Livestock from Consumption of Treated Water.				
Feedstuff	Endothall concentration in water (ppm)	Water consumption (kg/day)	Feed consumption (kg dry wt./day)[1]	Dietary Contribution from water (ppm)[2]
Beef cattle (feedlot cattle)	5.0	35	9.1	19.2
Dairy cattle (lactating cows)	5.0	218	24	45.4
Poultry (laying hens)	5.0	0.14	0.052	13.5
Swine (finishing hogs)	5.0	10	3.1	16.1

[1] Feed consumption from ChemSAC Memo, 6/30/2008.
[2] Contribution = (endothall concentration X water consumption/day) ÷ feed consumption/day.

Table 8. Calculation of Total (Feed Plus Water) Dietary Burdens of Endothall Residues to Livestock			
Feedstuff	Feed	Water	Total
Beef cattle (feedlot cattle)	8.9	19.2	28.1
Dairy cattle (lactating cows)	9.5	45.4	54.9
Poultry (laying hens)	3.6	13.5	17.1
Swine (finishing hogs)	4.0	16.1	20.1

Table 9. Calculation of estimated Residues in Livestock Tissues Based upon the TRR in the Metabolism Studies.		
Residues of Endothall in Dairy Cattle Tissues Based upon the Goat Metabolism Study		
Tissue	Total Radioactive Residues (ppm) after Feeding at 12.0 ppm	Anticipated Residues (ppm) after Feeding at 54.9 ppm
Milk.	0.006	0.028
Kidney	0.046	0.21
Liver	0.020	0.092
Muscle	0.005	0.023
Fat	0.002	0.009
Residues of Endothall in Beef Cattle Tissues, Sheep, Goats Based upon the Goat Metabolism Study		
Tissue	Total Radioactive Residues (ppm) after Feeding at 12.0 ppm	Anticipated Residues (ppm) after Feeding at 28.1
Kidney	0.046	0.108
Liver	0.020	0.047
Muscle	0.005	0.012
Fat	0.002	0.005
Residues of Endothall in Swine Tissues Based upon the Goat Metabolism Study		
Tissue	Total Radioactive Residues (ppm) after Feeding at 12.0 ppm	Anticipated Residues (ppm) after Feeding at 20.1 ppm
Kidney	0.046	0.077
Liver	0.020	0.034
Muscle	0.005	0.008
Fat	0.002	0.003
Residues of Endothall in Poultry Tissues Based upon the Chicken Metabolism Study		

Table 9. Calculation of estimated Residues in Livestock Tissues Based upon the TRR in the Metabolism Studies.

Tissue	Total Radioactive Residues (ppm) after feeding at 9.7 ppm	Anticipated Residues (ppm) after feeding at 17.1 ppm
Eggs	0.024	0.042
Yolk	0.024	0.042
White	0.002	0.004
Kidney and Other Meat Byproducts	0.088	0.16
Liver	0.021	0.037
Muscle	0.008	0.014
Fat	0.007	0.012

860.1500 Crop Field Trials

No new direct uses on crops are being proposed in the current petition; therefore, data requirements for crop field trials are not relevant to this petition. In addition, because of the high application rates the current data are expected to yield higher residues than would occur in crops rotated after a terrestrial use. Thus, these tolerances preempt the need for additional rotational crop studies.

860.1520 Processed Food and Feed

DP# D321179, D. Soderberg, 8/30/2005

47520701.de2.doc	(Sugar beet)	47520705.de2.doc	(Soybean)
47520706.de2.doc	(Tomato)	47520708.de2.doc	(Orange)
47520709.de2.doc	(Apple)	47520713.de2.doc	(Field corn, sorghum and wheat)
47520716.de2.doc	(Grape)	47520717.de2.doc	(Mint)
47520718.de2.doc	(Rice)		

Adequate cotton and potato processing studies are available supporting the direct use of endothall on these two crops as a defoliate/desiccant (DP# D321179, D. Soderberg, 8/30/2005). In the acceptable cotton processing study, cotton plants were treated with endothall as two broadcast foliar applications at rates totaling 3.2 lb ae/A (25-32x rate), with the second application being made 3 days prior to harvest. Endothall residues were 1.49 ppm in/on the undelinted cottonseed (RAC), which was then processed into hulls, meal and crude and refined oils. Endothall residues did not concentrate in hulls (0.36x), meal (0.22x), or refined oil (0.03x).

In the acceptable potato processing study, mature potato plants were treated with endothall (2 lb ae/gal) as two broadcast foliar applications at 5.0 lb ae/A, at RTI of 5 days, for a total of 10 lb ae/A (10x rate). Mature tubers harvested 7 days after the second application and processed into flakes, chips and wet peel. Endothall residues were 0.084 ppm in/on mature tubers, 0.088 ppm in flakes, 0.045 ppm in chips and 0.024 ppm in wet peel. These data indicate that endothall residues concentrated only slightly in flakes (1.04x) and were reduced in chips (0.54x) and wet peel (0.28x) fractions.

In support of the current petition for use of endothall-treated water on irrigated crops, IR-4 has submitted processing studies on apples, grapes, field corn, mint, oranges, rice, soybeans, sorghum, sugar beets, tomatoes and wheat. In each of these processing studies, endothall residues were determined using an adequate LC/MS/MS method (Method No. KP-242R1), which is described in the above Residue Analytical Methods Section. The method was validated in conjunction with each processing study, and the validated LOQ for endothall is 0.05 ppm in each RAC and processed fraction. Although endothall residues were reported to be <LOQ in/on several RACs and related processed fractions, review of the raw data indicated that endothall residues in/on these fractions were often just below the validated LOQ and were well above the estimated LODs. Therefore, when endothall residues were <LOQ in/on the RAC sample, residue values ≥LOD were used to calculated processing factors whenever possible.

The sample storage conditions and durations for the various RACs and processed fractions from each of the studies are supported by the available storage stability data. The details for each of the submitted processing studies are discussed below, and the resulting processing factors from each study are summarized in Table 10.

Table 10. Summary of Processing Factors for Endothall from Crops Irrigated with Endothall-treated water.

RAC	Processed Commodity	Application Rate [1]		PHI (days)	Processing Factor
		ppm	lb ae/A		
Apple [2]	Juice	5.0	6.79	0	1.2x
	Wet pomace				2.8x
Field Corn	Grits	5.0	6.77	0	NC [3]
	Meal				NC [1]
	Flour				NC [3]
	Refined oil (dry milling)				NC [3]
	Starch				NC [3]
	Refined oil (wet milling)				NC [1]
Grape	Juice	5.0	6.73	0	1.2x [5]
	Raisins				4.4x
Mint	Oil	5.0	6.64	0	<0.001x
Orange [2]	Dried pulp	5.0	6.63	0	2.2x
	Juice				0.7x
	Oil				<0.2x
Rice	Hulls	5.0	6.75	1	3.9x
	Bran				2.3x
	Polished rice				0.07x
Sorghum	Flour	5.0	6.77	0	0.7x
Soybean [2]	Hulls	5.0	6.77	0	3.9x
	Meal				0.8x
	Refined oil				<0.005x
Sugar beet	Dried pulp	5.0	6.79	0	1.1x
	Molasses				2.4x
	Refine sugar				<0.1x
Tomato [2]	Puree	5.0	6.77	0	2.1x [4]

Table 10.	Summary of Processing Factors for Endothall from Crops Irrigated with Endothall-treated water.				
RAC	Processed Commodity	Application Rate [1]		PHI (days)	Processing Factor
		ppm	lb ae/A		
	Paste				3.3x[4]
Wheat	Aspirated grain fractions (AGF)	5.0	6.71	0	15x
	Germ				2.6x
	Bran				2.3x
	Middlings				0.9x
	Flour				0.6x
	Shorts				1.4x

[1] The rate is expressed both in terms of the concentration in the irrigation water (ppm) and the total amount (lb ae/A) applied.
[2] Residue values <LLMV but ≥LOD were used for calculating processing factors.
[1] Residues were <LLMV and <LOD in/on field corn grain and each processed fraction. NC = not calculated.
[4] Residues were below the LLMV (<0.05 ppm) in both fruit and puree samples, but were well above the LOD at 0.002 ppm)
[1] 1.2x is the Maximum Theoretical Processing Factor for grape juice

Apple. In a field trial conducted in NY (Zone 1) during 2006, a monoalkylamine salt formulation of endothall (2.0 lb ae/gal SC/L) was used to treat the irrigation water at a rate of 5 ppm ae. The treated water was then applied using overhead sprinklers to the apple trees as six broadcast foliar applications during fruit development at a RTI of 7 days. A volume equivalent to 1 acre inch of water (~27,154 gal/A) was applied for each application. Based on the concentration of the endothall and the amount of water applied, the application rate for endothall was equivalent to 1.13 lb ae/A/application, for a total of 6.79 lb ae/A/season. Single bulk control and treated samples of apples were harvested at normal crop maturity, immediately following the last irrigation (0 DAT). The fruit was processed into juice and wet pomace using simulated commercial procedures.

Although endothall residues were <LOQ (<0.05 ppm) in/on whole fruits and juice, residues in these fractions were still above the estimated LOD (0.0025 ppm). Therefore, residue values >LOD were used to calculate the processing factors. Residues of endothall averaged 0.033 ppm in/on whole fruit (<LOQ) and were 0.041 ppm in juice and 0.091 ppm in wet pomace. The calculated processing factors were 1.2x for juice and 2.8x for wet pomace.

Based on HAFT residues of 0.039 ppm for apples, the maximum expected residues would be 0.047 ppm in juice and 0.109 ppm in wet pomace. As the recommended tolerance for pome fruits is 0.05 ppm, a separate tolerance for apple juice is not required, but a tolerance of 0.15 ppm is required for wet apple pomace.

Field corn. In a field trial conducted in IL (Zone 5) during the 2007, a monoalkylamine salt formulation of endothall (2 lb ae/gal SC/L) was used to treat the irrigation water at a rate of 5 ppm ae. The treated water was then applied using overhead sprinklers to field corn as six broadcast foliar applications during grain development and maturation at RTIs of 6-8 days. A volume equivalent to 1 acre inch of water (~27,154 gal/A) was applied for each application. Based on the concentration of the endothall in the irrigation water and the amount of water applied, the application rate for endothall was equivalent to 1.12-1.13 lb ae/A/application, for a total of 6.77 lb ae/A/season. Single bulk control and treated samples of mature corn grain was harvested on the day of the last irrigation (0 DAT), and the corn grain was processed into grits, meal, flour and oil by dry-milling and into starch and oil by wet-milling.

Following applications totaling 6.77 lb ae/A, endothall residues were <0.05 ppm (<LOQ) in/on the corn grain (RAC) and all its processed fractions. Although processing factors could not be determined for any processed corn fractions, there was no indication of endothall residues concentrating in processed corn commodities. Therefore, endothall are unlikely to occur in processed commodities derived from irrigated field corn.

Grape. In a field trial conducted in NY (Zones 1) during 2006, a monoalkylamine salt formulation of endothall (2 lb ae/gal SC/L) was used to treat the irrigation water at a rate of 5 ppm ae. The treated water was then applied using overhead sprinklers to the grapes as six broadcast foliar applications during fruit development at RTIs of 7 days. A total of ~1 acre inch of water (27,154 gal/A) was applied for each application. Based on the concentration of the endothall and the amount of water applied, the application rates for endothall were equivalent to 1.12 lb ae/A/application, for a total of 6.73 lb ae/A/season. Single bulk control and treated samples of grapes were harvested at normal crop maturity, immediately following the last irrigation (0 DAT), and the grapes were processed into juice and raisins using simulated commercial procedures.

Residues of endothall averaged 0.28 ppm in/on whole grapes (RAC) were 1.24 ppm in juice and 1.21 ppm in raisins. Thus, the processing factors calculated from these data for juice and raisins were 4.3x and 4.4x, respectively. However, the theoretical concentration factors for juice and raisins are 1.2x and 4.7x, respectively. Although the processing factor for raisins was in line with the theoretical value, the processing factor for juice was impossibly higher than the theoretical value. Therefore, the 1.2x factor will be used for assessing the need for grape juice tolerance (and in the dietary exposure assessment).

Based on HAFT residues of 0.642 ppm for grapes, the maximum expected residues would be 0.77 ppm in juice and 2.8 ppm in raisins. As the recommended tolerance for grapes is 0.9 ppm, a separate tolerance for grape juice is not required, but a tolerance of 3.0 ppm is required for raisins.

Mint. In a field trial conducted in WA (Zone 11) during 2006, a monoalkylamine salt formulation of endothall (2 lb ae/gal SC/L) was used to treat the irrigation water at a rate of 5 ppm ae. The treated water was then applied using overhead sprinklers to mint as six broadcast foliar applications during vegetative development at RTIs of 7 days. A volume equivalent to 1 acre inch of water (~27,154 gal/A) was applied for each application. Based on the concentration of the endothall in the irrigation water and the amount of water applied, the application rate for endothall was equivalent to 1.11 lb ae/A/application, for a total of 6.64 lb ae/A/season. Single bulk control and treated samples of mint tops were harvested at normal crop maturity, immediately following the last irrigation (0 DAT) and were processed into oil using simulated commercial procedures.

Following six overhead sprinkler applications of endothall to mint at rates totaling 6.64 lb ae/A, residues were 3.96 ppm in mint tops (RAC) and nondetectable (<0.0001 ppm) in mint oil, indicating that the processing factor of endothall in mint oil is <0.001x. As residues are reduced in mint oil, a separate tolerance for mint oil is not required.

Orange. In a field trial conducted in FL (Zone 3) during 2006, a monoalkylamine salt formulation of endothall (2 lb ae/gal SC/L) was used to treat the irrigation water at a rate of 5 ppm ae. The treated water was then applied using overhead sprinklers to the orange trees as six broadcast foliar applications during fruit development at RTIs of 5-6 days. A volume equivalent to 1 acre inch of water (~27,154 gal/A) was applied for each application. Based on the concentration of the endothall and the amount of water applied, the application rate for endothall was equivalent to 1.10 lb ae/A/application, for a total of 6.63 lb ae/A/season. Single bulk control and treated samples of oranges were harvested at normal crop maturity, immediately following the last irrigation (0 DAT). The fruit was processed into juice, oil and dried pulp using simulated commercial procedures.

Although endothall residues were <LOQ (<0.05 ppm) in/on whole orange fruits and in each processed fraction, residues above the estimated LOD (0.0025 ppm) were detected in each fraction except oil. Residues were detected at 0.019 ppm in/on whole fruit and at 0.014 ppm in juice, 0.041 ppm in dried pulp. Residues in oil were <LOD. Based on these residue values the processing factors were 0.7x for juice, 2.2x for dried pulp, and <0.2x for oil. The theoretical processing factors for citrus juice and oil are 2x and 1000x, respectively.

Based on HAFT residues of 0.026 ppm for oranges, the maximum expected residues would be 0.057 ppm dried pulp. As the recommended tolerance for citrus fruits is 0.05 ppm, a separate tolerance of 0.1 ppm is required for dried citrus pulp. Separate tolerances are not required for citrus juice and oil.

Rice. In a field trial conducted in TX (Zone 6) during 2007, a monoalkylamine salt formulation of endothall (2 lb ae/gal SC/L) was used to treat the irrigation water at a rate of 5 ppm ae. The treated water was then applied using overhead sprinklers to rice as six broadcast foliar applications during grain development and maturation at RTIs of 6-7 days. A volume equivalent to 1 acre inch of water (~27,154 gal/A) was applied for each application. Based on the concentration of the endothall in the irrigation water and the amount of water applied, the application rate for endothall was equivalent to 1.13 lb ae/A/application, for a total of 6.75 lb ae/A/season. Single bulk control and treated samples of rice grain were harvested at normal crop maturity, one day after the last irrigation (1 DAT), and processed into hulls, bran and polished rice using simulated commercial procedures.

Following six sprinkler applications of endothall at rates totaling 6.75 lb ae/A, residues in whole grain (RAC) were 0.872 ppm at 1 DAT, and the residues in the processed fractions were 0.60 ppm for polished rice, 3.44 ppm for hulls and 2.03 ppm for bran. The resulting processing factors were 0.07x for polished rice, 3.9x for hulls and 2.3x for bran. The theoretical processing factors for rice are 5x for hulls and 7.7x for bran.

Based on HAFT residues of 1.18 ppm for rice grain, the maximum expected residues would be 4.6 ppm for hulls and 1.48 ppm for bran. As the recommended tolerance for cereal grains is 3.0 ppm, a separate tolerance for rice bran is not required, but a tolerance of 5.0 ppm is required for rice hulls.

Sorghum. In a field trial conducted in KS (Zone 7) during 2007, a monoalkylamine salt formulation of endothall (2 lb ae/gal SC/L) was used to treat the irrigation water at a rate of 5 ppm ae. The treated water was then applied using overhead sprinklers to the sorghum crop as six broadcast foliar applications during grain development and maturation at RTIs of 6-8 days. A volume equivalent to 1 acre inch of water (~27,154 gal/A) was applied for each application. Based on the concentration of the endothall in the irrigation water and the amount of water applied, the application rate for endothall was equivalent to 1.12-1.13 lb ae/A/application, for a total of 6.77 lb ae/A/season Single bulk control and treated samples of mature sorghum grain were harvested on the day of the last irrigation (0 DAT), and the grain samples processed into flour using simulated commercial procedures.

Endothall residues were 1.49 ppm in/on sorghum grain (RAC) and 1.09 ppm in sorghum flour, indicating that residues were reduced in flour by 0.7x. Therefore, separate tolerance is not required for sorghum flour.

Soybean. In a field trial conducted in IA (Zone 5) during 2007, a monoalkylamine salt formulation of endothall (2 lb ae/gal SC/L) was used to treat the irrigation water at a rate of 5 ppm ae. The treated water was then applied using overhead sprinklers to soybeans as six broadcast foliar applications during seed and pod development at RTIs of 6-8 days. A volume equivalent to 1 acre inch of water (~27,154 gal/A) was applied for each application. Based on the concentration of the endothall in the irrigation water and the amount of water applied, the application rate for endothall was equivalent to 1.13 lb ae/A/application, for a total of 6.77 lb ae/A/season. Single bulk control and treated samples of soybeans were harvested at normal crop maturity, immediately following the last irrigation (0 DAT). The soybeans were processed into hulls, meal and refined oil using simulated commercial procedures.

Following six overhead sprinkler applications of endothall (monoalkylamine salt) to soybeans at rates totaling 6.77 lb ae/A, endothall residues were 0.021 ppm (<LOQ) in/on whole seeds, 0.083 ppm in/on hulls, 0.017 ppm in meal, and nondetectable (<0.0001 ppm) in refined oil. The processing factors were 3.9x for hulls, 0.8x for meal, and <0.005x for oil. The theoretical processing factors for soybean commodities are 11.3x for hulls, 2.2x for meal, and 12x for oil.

Based on HAFT residues of 0.07 ppm for soybeans, the maximum expected residues would be 0.273 ppm for hulls. As the recommended tolerance for soybean seeds is 0.2 ppm, a separate tolerance of 0.3 ppm is required for soybean hulls.

Sugar beet. In a field trial conducted in CA (Zones 10) during 2007, a monoalkylamine salt formulation of endothall (2 lb ae/gal SC/L) was used to treat the irrigation water at a rate of 5 ppm ae. The treated water was then applied using overhead sprinklers to the sugar beets as six broadcast foliar applications during vegetative development at RTIs of 7-8 days. A volume equivalent to 1 acre inch of water (~27,154 gal/A) was applied for each application. Based on the concentration of the endothall and the amount of water applied, the application rate for endothall was equivalent to 1.13 lb ae/A/application, for a total of 6.79 lb ae/A/season. Single bulk control and treated samples of sugar beet roots were harvested at normal crop maturity, immediately following the last irrigation (0 DAT). The roots were washed and processed into dried pulp, molasses, and refined sugar using simulated commercial procedures.

Residues of endothall averaged 0.493 ppm in/on whole unwashed roots (RAC) and were 0.554 ppm in dried pulp, 1.203 in molasses, and <0.05 ppm in refined sugar. The processing factors were 1.1x for dried pulp, 2.4x for molasses, and <0.1x for refined sugar. The theoretical concentration factor for refined sugar is 12.5x.

Based on HAFT residues of 0.493 ppm for sugar beet roots, the maximum expected residues would be 0.542 ppm for dried pulp and 1.18 ppm in molasses. As the recommended tolerance for root and tuber vegetables is 1.0 ppm, a separate tolerance is not required for dried pulp, but a tolerance of 1.2 ppm is required for sugar beet molasses.

Tomato. In a field trial conducted in FL (Zone 3) during 2006, a monoalkylamine salt formulation of endothall (2 lb ae/gal SC/L) was used to treat the irrigation water at a rate of 5 ppm ae. The treated water was then applied using overhead sprinklers to tomatoes as six broadcast foliar applications during fruit development at RTIs of 8 days. A volume equivalent to 1 acre inch of water (~27,154 gal/A) was applied for each application. Based on the concentration of the endothall in the irrigation water and the actual amount of water applied, the application rate for endothall was equivalent to 1.13 lb ae/A/application, for a total of 6.77 lb ae/A/season. Single bulk control and treated samples of tomatoes were harvested at normal crop maturity, immediately following the last irrigation (0 DAT). The tomatoes were processed into puree and paste using simulated commercial procedures.

Residues of endothall were formally reported to be <0.05 ppm in/on whole fruits and puree and 0.069 ppm in tomato paste. However, page 81 of the report indicated that detectable residues (≥0.002 ppm) were present in whole fruit at 0.021 ppm, 0.044 ppm in the puree, and 0.069 in the paste. Since the residues in the puree seemed no less likely to be reasonable estimates than those on the raw fruit or in the puree (all are below the LLMV, but above the LOD. We have used these numbers to estimate factors of 2.1x for puree and 3.3x for the paste. These numbers make reasonable sense when compared to the mass balance calculations. EPA's published theoretical processing factors for tomato puree and paste are 1.4 and 5.5x, respectively.

Both processing factors lead to values above the recommended tolerance. Therefore, a separate tolerance of 0.1 ppm is required for both tomato puree and tomato paste.

Wheat. In a field trial conducted in TX (Zone 6) during 2007, a monoalkylamine salt formulation of endothall (2 lb ae/gal SC/L) was used to treat the irrigation water at a rate of 5 ppm ae. The treated water was then applied using overhead sprinklers to the wheat crop as six broadcast foliar applications during grain development and maturation at RTIs of 6-8 days. A volume equivalent to 1 acre inch of water (~27,154 gal/A) was applied for each application. Based on the concentration of the endothall in the irrigation water and the amount of water applied, the application rate for endothall was equivalent to 1.12-1.13 lb ae/A/application, for a total of 6.71 lb ae/A/season. Single bulk control and treated samples of mature wheat grain were harvested at normal maturity, on the day of the last irrigation (0 DAT). The wheat grain was initially cleaned to generate AGF and was then milled using simulated commercial procedures into germ, bran, middlings, shorts and flour.

Endothall residues were 1.34 ppm in/on the bulk sample of wheat grain and 20.3 ppm in/on the composited AGF sample, for a concentration factor of 15x for wheat AGF. Following processing, endothall residues were 3.44 ppm in germ, 3.10 ppm in bran, 1.14 ppm in middlings, 0.75 ppm in flour, and 1.81 ppm in shorts. The resulting processing factors were 2.6x for germ, 2.3x for bran, 0.9x for middlings, 0.6x for flour, and 1.4x for shorts.

Based on HAFT residues of 1.91 ppm for wheat grain, the maximum expected residues would be 28.7 ppm for AGF, 4.97 ppm for germ, 4.39 ppm for bran and 2.67 ppm for shorts. Because residues in shorts are below the recommended 3 ppm tolerance for cereal grains, a separate tolerance in not required for shorts. However, a tolerance of 5.0 ppm in required on wheat milled byproducts to cover residues in wheat germ and bran. In addition, a 30 ppm tolerance is required for grain AGF.

Conclusions. The submitted processing studies for irrigated crops are adequate, and cover all the crops requested in the Endothall RED. The appropriate processed fractions were generated in each study, and endothall residues in each RAC and processed commodity were determined using an adequate LC/MS/MS method. The sample storage conditions and durations are also supported by the available storage stability data. With the exception of field corn grain, detectable residues of endothall were found in all RAC samples. HED notes that although residues were reported to be <0.05 ppm (<LOQ) in the apple, orange, soybean and tomato samples used for processing, endothall residues were detectable in each of these RACs at 0.019-0.033 ppm. Therefore, these detectable residues were used for calculating processing factors for these crops.

Endothall residues were shown to concentrate in the following processed fractions: apple juice (1.2x) and wet pomace (2.8x), grape raisins (4.4x), dried citrus pulp (2.2x), rice hulls (3.9x) and bran (2.3x), soybean hulls (3.9x), sugar beet molasses (2.4x) and dried pulp (1.1x), tomato paste (3.3x), and wheat germ (2.6x), bran (2.3x) and shorts (1.4x). (Although grape juice had an apparent concentration factor of 4.3x, HED used the maximum theoretical processing factor for grape juice (1.2x) to assess the need for a separate grape juice tolerance.)

Based on the above processing factors and the HAFT residues for the various RACs, the maximum expected residues in various processed commodities exceeded the tolerance recommended for the associated RAC. Therefore, separate tolerances are required for the following processed commodities at the recommended levels: apple wet pomace (0.15 ppm), raisins (3 ppm), dried citrus pulp (0.1 ppm), rice hulls (5 ppm), soybean hulls (0.3 ppm), sugar beet molasses (1.2 ppm), tomato paste (0.1 ppm), and wheat milled byproducts (5 ppm).

Although no processing studies are available for oilseed crops (canola, flax, safflower, and sunflower), the available soybean processing study is adequate for assessing the potential for concentration of endothall in oil seed meal and refined oil for purposes of this petition. The soybean processing data indicate that endothall residues are unlikely to concentrate in meal and oil fractions from other oil seed crops.

In addition, wheat processing study showed that residues concentrated in AGF by 15x indicating that a separate tolerance will be required for AGF. Because endothall residues were higher in wheat grain than in the other major grains (field corn, soybean and sorghum), the HAFT for wheat grain (1.91 ppm) was used to calculate the maximum expected residues for AGF (28.7 ppm). These data indicate that a tolerance of 30 ppm would be appropriate for AGF.

860.1650 Submittal of Analytical Reference Standards

An analytical standard for endothall is currently available in the EPA National Pesticide Standards Repository (personal communication with Dallas Wright, ACB, 10/23/08), with an expiration date of 12/28/2012. Analytical reference standards must be replenished as requested by the Repository.

Analytical standards of the monomethyl and dimethyl esters are required to be submitted. The reference standards should be sent to the Analytical Chemistry Lab, which is located at Fort Meade, to the attention of either Theresa Cole or Thuy Nguyen at the following address:

USEPA
National Pesticide Standards Repository/Analytical Chemistry Branch/OPP
701 Mapes Road
Fort George G. Meade, MD 20755-5350

860.1850/1900 Confined and Field Accumulation in Rotational Crops

DP# D321179, D. Soderberg, 8/30/2005

Although the available confined rotational crop study was deemed inadequate, HED has concluded that based upon the results of the plant metabolism data and of soil and water metabolism data, it is possible to infer that the only possible residues of significance in rotated crops are endothall and its mono methyl and dimethyl esters. Therefore, a new confined rotational crop study is no longer required so long as limited field trials are performed that measure all three of endothall, and the monomethyl- and dimethyl- esters of endothall.

Although the Endothall RED required data from limited field rotational crop trials, the inadvertent exposure of crops to endothall via the use of treated irrigation water will clearly exceed the potential secondary exposure of crops planted in rotation with endothall treated crops such as cotton and potatoes. Therefore, the establishment of tolerances for indirect/inadvertent residues of endothall on the proposed irrigated crops supersedes the need for limited field rotational trial data or the need for rotational crop tolerances.

860.1550 Proposed Tolerances

The residues of concern for endothall for purposes of both risk assessment and tolerance enforcement in plant and animal commodities include parent endothall and its monomethyl ester. Permanent tolerances are currently established for the combined residues of endothall and its monomethyl ester at 0.1 ppm in/on cotton seeds, fish, dried hops and potatoes, and at 0.05 ppm in/on rice grain and straw [40 CFR §180.293(a)(1)]. An interim tolerance of 0.2 ppm has also been established for endothall acid in potable water resulting from the use of the monoalkylamine or dipotassium salts of endothall for control of aquatic plants in canals, lakes, ponds and other potential water sources. An interim tolerance has also been established for endothall on sugar beet at 0.2 ppm [40 CFR §180.319].

The available field trial data are adequate for purposes of assessing inadvertent residues of endothall on irrigated crops. Although the residue data available on any given crop is limited, the field trials are likely to represent a very conservative estimate of endothall residues on irrigated crops. This is not only because crops are (properly) treated at the maximum use rate and the maximum number of times per season, but also because overhead irrigation was used and because a short PHI (0-DAT) used in each field trial. The occurrence of phytotoxicity on a number of the crops tested also make it unlikely that repeated irrigation with water containing high levels of endothall (5 ppm) will go unrecognized and be allowed to occur under normal agricultural conditions.

In calculating recommended tolerances for irrigated crops, HED has not utilized the NAFTA MRL Calculator (or Tolerance Harmonization Spreadsheet) except for grass commodities, corn grain and soybeans. The residues are already expected to be very conservative. In addition, only a very limited number of field trials were performed for any crop/crop group, and there was only one plot for each field trial. Thus, in some cases there was only a single plot tested for a crop/crop group. Correct use of the NAFTA MRL Calculator given these limited data would add an unrealistically large additional conservative factor onto these already conservative results, and results would have less reliability given the limited number of values use for each distribution. In addition, several tolerances are based upon residues detected below the LOQ of the method, but above the LOD. These residues cannot be considered to be non-detectable, but the precision of determination of residues in this range is larger than normally attributed to the method, and results are usually biased high due to undue influence of background contribution to the responses. Given all of this, given that these tolerances are for inadvertent residues and therefore in many cases are based upon very broad translations of data, sometimes even across crop groups, HED has concluded that it makes better sense to estimate tolerances using a more practical, common sense approach. In most cases these tolerances are approximately twice the highest results from the highest residues/plot tested.

The proposed tolerances for irrigated crops are listed in Table 10, along with the Agency's recommended tolerances. As the tolerances on irrigated crops are for inadvertent residues, they should be established under 40 CFR §180.293(d). Substantial changes in the proposed tolerances are noted below.

IR-4 provided residue data on cabbage to support the tolerance on Brassica leafy vegetables. However, because mustard greens typically have higher residues than cabbage, the leaf lettuce field trial data were used to assess the tolerance on Brassica leafy vegetables.

For legume vegetables, the available field trial data indicated that a single crop group tolerance is not appropriate. Therefore, HED is recommending that separate tolerances be established for the three legume vegetable subgroups (6A, 6B and 6C), along with a tolerance on soybean seeds. In addition, IR-4 did not propose a tolerance for the foliage of legumes (group 7). HED is recommending a tolerance for legume foliage based on the alfalfa field trial data.

Tolerances for okra, pistachios and herbs (subgroup 19A) are being recommended based on the respective field trial data for tomatoes, tree nuts and mint.

For cereal grains, IR-4 proposed tolerances for cereal grains (except rice); however, the available residue data indicate that residues for rice grain are similar to wheat and sorghum grain, while residues in/on corn (field and sweet) are substantially lower. Therefore, HED is recommending a crop group tolerance for cereal grain, except corn, and establishing separate tolerances for field and pop corn grain and sweet corn K+CWHR.

Although IR-4 did not propose tolerances on any processed crop fractions, the available field trial and processing data indicate that separate tolerances are required for the following processed commodities at the recommended levels: apple wet pomace (0.15 ppm), raisins (3 ppm), dried citrus pulp (0.1 ppm), rice hulls (5 ppm), soybean hulls (0.3 ppm), sugar beet molasses (1.2 ppm), tomato paste (0.1 ppm), and wheat milled byproducts (5 ppm). A separate tolerance is also AGF at 30 ppm.

There are currently no established Codex, Canadian, or Mexican maximum residue limits (MRLs) for endothall on plant or animal commodities. Therefore, there are no issues related to harmonization with international MRLs.

Table 11. Tolerance Summary for Endothall.

Commodity	Proposed Tolerance (ppm)	Recommended Tolerance (ppm)	Comments; *Correct Commodity Definition*
40 CFR §180.293(d)			
Vegetable, root and tuber, group 1	2	1.0	Based on maximum residues in sugar beets (0.493 ppm), carrots (0.088 ppm) and potatoes (0.103 ppm)
Beet, sugar, molasses	None	1.5	Maximum expected residues are 1.18 ppm in molasses based on HAFT residues of 0.493 ppm in sugar beet roots and a 2.4x processing factor.
Vegetable, leaves of root and tuber, group 2	3.5	3.0	Based on maximum residues in sugar beet tops (1.62 ppm)
Vegetable, bulb, group 3	2	0.5	Based on maximum residues in green onions (0.26 ppm) and dry bulb onions (<0.05 ppm)
Vegetable, leafy, except brassica, group 4	3.5	2.0	Based on maximum independent plot residues in leaf lettuce (0.99 ppm) and head lettuce (0.60 ppm)
Vegetable, brassica, group 5	0.1	None	Based upon Cabbage HAFT of 0.063 ppm)
Vegetable, brassica, head and stem subgroup 5A	None	0.1	Based upon Cabbage HAFT of 0.063 ppm)
Vegetable, brassica, leafy, group 5B	None	2	Based upon maximum residues in leaf lettuce, which better represents residues on leafy Brassica than does cabbage.
Vegetable, legume, group 6	3	None	Separate tolerances should be established for soybeans and the various legume subgroups based on the maximum residues in succulent beans (0.47 ppm) and succulent peas (0.94 ppm), and those in dried beans (0.12 ppm), and on soybeans (0.07 ppm). Soybean seed
Vegetable, legume, edible podded, subgroup 6A and Pea and bean, succulent shelled, subgroup 6B	None	2.0	

Table 11. Tolerance Summary for Endothall.			
Commodity	Proposed Tolerance (ppm)	Recommended Tolerance (ppm)	Comments; *Correct Commodity Definition*
40 CFR §180.293(d)			
Pea and bean, dried shelled, subgroup 6C	None	0.2	tolerance (4 trials) is based upon tolerance spreadsheet.
Soybean seed	None	0.2	
Soybean, hulls	None	0.5	Maximum expected residues are 0.27 ppm in hulls based on HAFT residues of 0.07 ppm in soybeans and a 3.9x processing factor.
Vegetable, foliage of legume, group 7	None	4	Based on maximum residues in alfalfa forage
Vegetable, fruiting, group 8	0.05	0.05	Based on maximum residues in tomatoes (<0.05 ppm).
Okra	None	0.05	
Tomato, paste	None	0.1	Maximum expected residues are 0.069 ppm in paste based on HAFT residues of 0.021 ppm in tomatoes and a 3.3x processing factor for paste.
Tomato, puree	None	0.1	Maximum expected residues are 0.044 ppm in paste based on HAFT residues of 0.021 ppm in tomatoes and a 2.1x processing factor for puree.
Vegetable, cucurbit, group 9	1.1	1.5	Based on maximum residues in cucumbers (0.74 ppm).
Fruit, citrus, group 10	0.05	0.05	Based on maximum residues in oranges (<0.05 ppm).
Citrus, dried pulp	None	0.1	Maximum expected residues are 0.057 ppm in dried pulp based on HAFT residues of 0.026 ppm in oranges and a 2.2x processing factor.
Fruit, pome, group 11	0.05	0.05	Based on maximum residues in apples (<0.05 ppm).
Apple, wet pomace	None	0.15	Maximum expected residues are 0.109 ppm in wet pomace based on HAFT residues of 0.039 ppm in apples and a 2.8x processing factor.
Fruit, stone, group 12	0.25	0.3	Based on maximum residues in peaches (0.15 ppm).
Canebery subgroup 13-07A and bushberry subgroup 13-07B	0.6	0.6	Based on maximum residues in blueberries (0.18 ppm) and blackberries (0.33 ppm).
Grape	0.9	1.0	Based upon maximum residues on grapes (0.64 ppm).
Grape, raisin	None	5.0	Maximum expected residues are 2.8 ppm in raisins based on HAFT residues of 0.64 ppm in grapes and a 4.4x processing factor.

Table 11. Tolerance Summary for Endothall.			
Commodity	Proposed Tolerance (ppm)	Recommended Tolerance (ppm)	Comments; *Correct Commodity Definition*
40 CFR §180.293(d)			
Nut, tree, group 14	0.05	0.05	Based on maximum residues in almond and pecan nutmeats (<0.05 ppm).
Pistachio	None	0.05	
Almond, hulls	10	15	Based on maximum residues in hulls (8.2 ppm).
Grain, cereal, group 15, except corn	1.9	4	The available data support a crop group tolerance, except for corn
Corn, sweet, kernel plus cob with husks removed	None	0.3	Tolerance based on maximum residues in sweet corn K+CWHR (0.17 ppm)
Corn, field, grain	None	0.07	Tolerance based on tolerance spreadsheet for corn grain
Corn, pop, grain	None	0.07	
Cereal, forage, fodder and straw, group 16, hay	5.0	None	Combined into Forage, Hay and Straw
Cereal, forage, fodder and straw, group 16, straw	6	None	Combined into Forage, Hay and Straw
Cereal, forage, fodder and straw, group 16, forage	3.5	None	Combined into Forage, Hay and Straw
Cereal, forage, fodder and straw, Group 16, except stover	3.5	6	Based on maximum residues on various forages (2.7) and wheat hay and straw. Note that field corn, sorghum and wheat forages received only 2-3 applications prior to harvest (0.3-0.5x rate).
Cereal, forage, fodder and hay, group 16, stover	11	10	Based on adequate data from field corn and sorghum stover (max 5.0 ppm).
Grain, aspirated fractions	24	35	Maximum expected residues in AGF are 29 ppm based on HAFT residues of 1.9 ppm for wheat grain and a concentration factor of 15x for AGF.
Grass, forage, fodder, and hay, group 17, forage	3	3.5	Based upon tolerance spreadsheet (6 trials)
Grass, forage, fodder, and hay, group 17, hay	19	18	Based upon tolerance spreadsheet (6 trials)
Animal feed, Nongrass, group 18, forage	3.5	4.0	Based on maximum residues in alfalfa forage (2.1 ppm) and hay (4.9 ppm)
Animal feed, Nongrass, group 18, hay	8	10	
Peppermint, tops	7	5	Based on maximum residues in mint tops (2.8 ppm).
Spearmint, tops	7	5	
Herb and spice, group 19	None	5	
Rice, grain	1.7	None	Separate tolerances are not required for rice grain and straw as these commodities are covered by the tolerances on cereal grains and cereal grain straw.
Rice, straw	4.5	None	

Table 11. Tolerance Summary for Endothall.			
Commodity	Proposed Tolerance (ppm)	Recommended Tolerance (ppm)	Comments; *Correct Commodity Definition*
40 CFR §180.293(d)			
Rice, hulls	None	8	Based on HAFT residues of 1.0 ppm for rice grain and a processing factor of 3.9x for hulls, the maximum expected residues in rice hulls is 4.0 ppm.
Wheat, milled byproducts	None	5	Based on HAFT residues of 1.9 ppm for wheat grain and processing factors of 2.6x for germ, and 2.3x for bran, and 1.4x for shorts, the maximum expected residues in milled byproducts is 5.0 ppm.
Food commodities	None	5	Inadvertent residues on any food crop/commodity not included within the assigned crop groups and miscellaneous tolerances. Based upon Mint.
Feed commodities	None	10	Inadvertent residues on any feed crop/commodity not included within the assigned crop groups and miscellaneous tolerances. Based upon Cereal Grains.
Cattle, muscle	None	0.03	Based upon calculations for Dairy Cattle using metabolism data.
Cattle, kidney	None	0.20	Based upon calculations for Dairy Cattle using metabolism data.
Cattle, liver	None	0.10	Based upon calculations for Dairy Cattle using metabolism data.
Cattle, fat	None	0.01	Based upon calculations for Dairy Cattle using metabolism data.
Milk	None	0.03	Based upon calculations for Dairy Cattle using metabolism data.
Sheep, muscle	None	0.015	Based upon calculations for Beef Cattle using metabolism data.
Sheep, kidney	None	0.15	Based upon calculations for Beef Cattle using metabolism data.
Sheep, liver	None	0.05	Based upon calculations for Beef Cattle using metabolism data.
Sheep, fat	None	0.005	Based upon calculations for Beef Cattle using metabolism data.
Goat, muscle	None	0.015	Based upon calculations for Beef Cattle using metabolism data.
Goat, kidney	None	0.15	Based upon calculations for Beef Cattle using metabolism data.
Goat, liver	None	0.05	Based upon calculations for Beef Cattle using metabolism data.
Goat, fat	None	0.005	Based upon calculations for Beef Cattle using metabolism data.
Hog, muscle	None	0.01	Based upon calculations using metabolism data.
Hog, kidney	None	0.10	Based upon calculations using metabolism data.

Table 11. Tolerance Summary for Endothall.			
Commodity	Proposed Tolerance (ppm)	Recommended Tolerance (ppm)	Comments; *Correct Commodity Definition*
40 CFR §180.293(d)			
Hog, liver	None	0.05	Based upon calculations using metabolism data.
Hog, fat	None	0.005	Based upon calculations using metabolism data.
Poultry, muscle	None	0.015	Based upon calculations using metabolism data.
Poultry, liver	None	0.05	Based upon calculations using metabolism data.
Poultry, fat	None	0.015	Based upon calculations using metabolism data.
Poultry, meat byproducts	None	0.20	Based upon calculations using metabolism data.
Egg	None	0.05	Based upon calculations using metabolism data.

References

DP Number: D321179
Subject: Endothall and its Salts. Residue Chemistry Considerations for Reregistration Eligibility Decision. Revised per Registrant Comments.
From: D. Soderberg
To: R. Zendzian
Dated: 8/30/2005
MRID(s): None

Attachments:
Attachment 1. Table of Individual Residue Values Found for Each Different Commodity
Attachment 2: Tolerance Spreadsheet analyses for Commodities with Four or More Field Trials

Residue Data for Endothall								
Trial ID (City, State; Year)	Zone	Crop; Variety	Matrix	Total Rate[4]		PHI (days)	Residues (ppm)[5,6]	
				ppm	lb ae/A			
TABLE C.3. Residue Data from Root and Tuber Vegetable Field Trials with Endothall.								
Sugar Beets								
Conklin, MI 2007 MI$19	5	Sugar beet; Beta 5451	Tops	5.0	6.77	0	1.256	1.374
				3.5	4.80	0	0.523	0.531
			Roots	5.0	6.77	0	0.199	0.136
				3.5	4.80	0	0.120	0.115
Arroyo Grande, CA 2007 CA$22	10	Sugar beet; Alpine Medium Quickprime	Tops	5.0	6.79	0	1.618	1.105
				3.5	4.88	0	1.279	0.948
			Roots	5.0	6.79	0	0.591	0.395
				3.5	4.88	0	0.345	0.316
Carrot								
Ravenna, MI 2007 MI$20	5	Carrot; Recoleta	Root	5.0	6.77	0	0.075	0.062
Arroyo Grande, CA 2006 CA$06	10	Carrot; Nantes	Root	5.0	6.79	0	0.088	0.088
Potato								
Conklin, MI 2007 MI$21	5	Potato; Dark Red Norland	Tuber	5.0	6.77	0	0.072	0.103
Payette, ID 2007 ID$23	11	Potato; Ranger Russet	Tuber	5.0	6.83	0	0.067	0.078
TABLE C.3. Residue Data from Onion Field Trials with Endothall (SC/L).								
East Bernard, TX 2007 TX$07	6	Green Onion; Evergreen Hardy White	Whole plant without roots	5.0	6.75	0	0.284	0.234
Arroyo Grande, CA 2007 CA$18	10	Dry Bulb Onion; Onion Yellow Granex F1	Dry Bulb	5.0	6.76	0	*0.023*[1]	*0.023*[1]

Residue Data for Endothall								
Trial ID (City, State; Year)	Zone	Crop; Variety	Matrix	Total Rate[4]		PHI (days)	Residues (ppm)[5,6]	
				ppm	lb ae/A			
TABLE C.3. Residue Data from Lettuce Field Trials with Endothall Salts (SC/L).								
Leaf Lettuce								
Arroyo Grande, CA 2006 CA$04	10	Leaf lettuce; Greenslar	Leaves	5.0	6.76	0	0.743	1.240
				3.5	4.81	0	0.582	1.013
North Rose, NY 2007 NY$28	1	Leaf Lettuce; Green salad bowl	Leaves	5.0	6.73	0	0.462	0.410
				3.5	4.67	0	0.255	0.241
Head Lettuce								
Arroyo Grande, CA 2006 CA$05	10	Head Lettuce; Snaiper	Heads, w/wrapper leaves	5.0	6.76	0	0.092	0.081
				3.5	4.81	0	*0.032*[1]	0.082
Lyons, NY 2007 NY$31	1	Head Lettuce; Ithaca MTO	Heads, w/wrapper leaves	5.0	7.17	0	0.604	0.491
				3.5	5.07	0	0.582	0.436
TABLE C.3. Residue Data from Cabbage Field Trials with Endothall (SC/L).								
North Rose, NY 2006 NY$23	1	Matsumo	Head with wrapper leaves	5.0	7.00	0	*0.025*[1]	0.075
Baptistown, NJ 2006 NJ$08	1	Blue Lagoon	Head with wrapper leaves	5.0	5.64	0	0.065	0.058
TABLE C.3. Residue Data from Legume Field Trials with Endothall Monoamine Salt (SC/L).								
Succulent Podded Beans								
Arroyo Grande, CA 2007 CA$26	10	Succulent Lima /speckled	Succulent seed w/pod	5.0	9.02	0	0.414	0.521
Baptistown, NJ 2006 NJ$24	1	Succulent Lima/ Burpee's Improved Bush	Succulent seed w/pod	5.0	6.75	0	0.291	0.324
Dried Beans								
Delavan, WI 2007 WI$13	5	Dry bean/ Pinto	Dried seed	5.0	6.77	0	0.134	0.070
Richland, IA 2007 IA$14	5	Dry bean/ Great Northern	Dried seed	5.0	6.77	0	0.109	0.123
Succulent Podded Peas								
Ephrata, WA 2007 WA$17	12	Succulent pea/ Tonic	Succulent seed w/pod	5.0	6.74	0	0.878	1.00
Delavan, WI 2007 WI$12	5	Succulent pea/ Wanto	Succulent seed w/pod	5.0	6.74	0	0.537	0.522
Soybean								
Baptistown, NJ 2006 NJ$25	1	Soybean/ 93244449	Dried seed	5.0	6.75	1	0.072	0.068
Newport, AR 2007 AR$16	4	Soybean/ BPR 5423 nRR	Dried seed	5.0	6.76	0	*0.017*[1]	ND[2]

Residue Data for Endothall

Trial ID (City, State; Year)	Zone	Crop; Variety	Matrix	Total Rate[4]		PHI (days)	Residues (ppm)[5,6]	
				ppm	lb ae/A			
Richland, IA 2007 IA$15	5	Soybean/ 93M42	Dried seed	5.0	6.77	0	0.020[1]	0.017[1]
Sparta, IL 2007 IL$11	5	Soybean/ Asgrow AG 3905	Dried seed	5.0	6.77	0	0.038[1]	0.026[1]
TABLE C.3. Residue Data from Tomato Field Trials with Endothall Monoamine Salt (SC/L).								
Grande Arroyo, CA 20006 CA$28	10	Tomato/ Organic Yaqui	Fruit	5.0	6.74	0	NR[3]	NR[3]
Oviedo, FL 2006 FL$27	3	Tomato/ Celebrity	Fruit	5.0	6.77	0	0.027[1]	0.030[1]
TABLE C.3. Residue Data from Cucumber Field Trials with Endothall Salts (SC/L).								
Baptistown, NJ 2006 NJ$02	1	Burpless bush	Fruit	5.0	6.75	0	0.738	0.738
				3.5	4.80	0	0.406	0.459
Conklin, MI 2007 MI$42	5	Fancipack	Fruit	5.0	6.77	0	0.234	0.284
				3.5	4.81	0	0.337	0.310
TABLE C.3. Residue Data from Orange Field Trials with Endothall Monoamine Salt (SC/L).								
Dinuba, CA 2006 CA$11	10	Rush Thompson Improved	Fruit	5.0	6.78	0	0.024[1]	0.028[1]
Oviedo, FL 2006 FL$10	3	Hamlin	Fruit	5.0	6.63	0	0.022[1]	0.021[1]
TABLE C.3. Residue Data from Apple Field Trials with Endothall Monoamine Salt (SC/L).								
North Rose, NY 2006 NY$29	1	Empire	Fruit	5.0	6.79	0	0.031[1]	0.047[1]
Ephrata, WA 2006 WA$16	11	Braeburn	Fruit	5.0	6.64	0	ND[2]	0.043[1]
TABLE C.3. Residue Data from Peach Field Trials with Endothall Salts (SC/L).								
Morven, GA 2007 GA$01	2	White	Fruit	5.0	7.08	0	0.045[1]	0.043[1]
				3.5	5.05	0	0.043[1]	0.046[1]
Dinuba, CA 2007 CA$02	10	Snow Princess	Fruit	5.0	6.78	0	0.144	0.160
				3.5	4.82	0	0.118	0.136
TABLE C.3. Residue Data from Crop Field Trials with Endothall Monoamine Salt (SC/L).								
Conklin, MI 2007 MI$32	5	Blueberry: Blue Ray (Highbush)	Fruit	5.0	6.77	0	0.158	0.197
Hillsboro, OR 2007 OR$41	12	Blackberry (Boysen)	Fruit	5.0	6.73	0	0.311	0.346
TABLE C.3. Residue Data from Tree Nut Field Trials with Endothall Monoamine Salt (SC/L).								
Irwinville, GA 2006 GA$22	2	Pecan; summer	Nutmeat	5.0	7.01	0	ND[2]	0.024[1]
Coalinga, CA	10	Almond;	Nutmeat	5.0	6.80	0	0.036[1]	0.037[1]

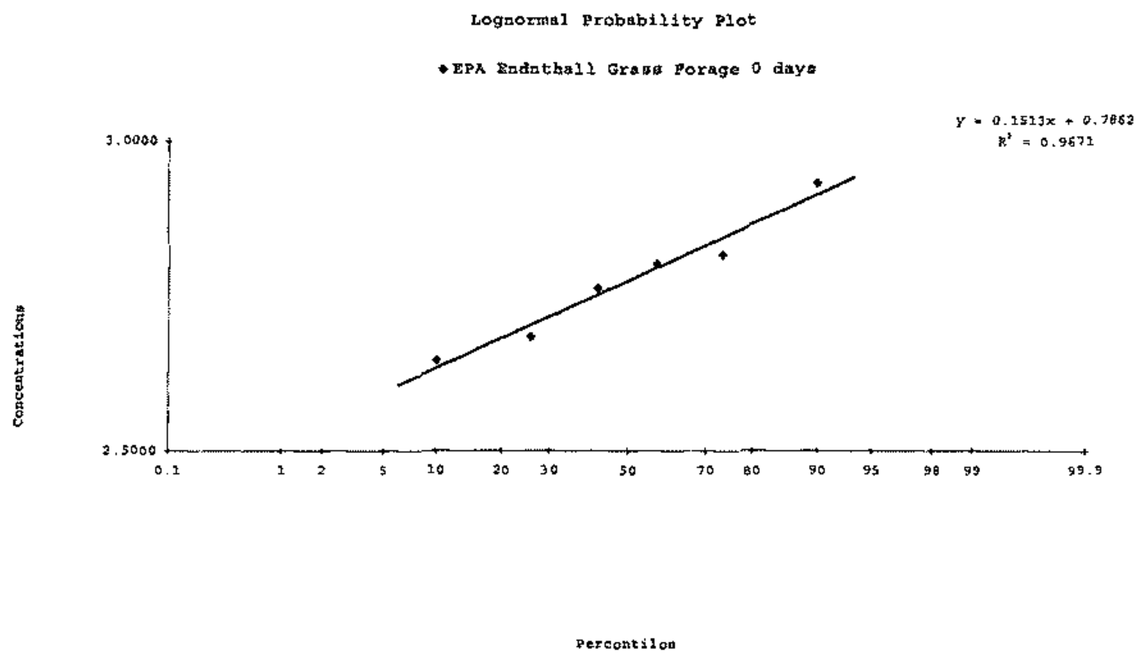
Residue Data for Endothall								
Trial ID (City, State; Year)	Zone	Crop; Variety	Matrix	Total Rate[4]		PHI (days)	Residues (ppm)[5,6]	
				ppm	lb ae/A			
2007 CA$40		nonpariel	Hulls				6.91	8.20
TABLE C.3. Residue Data from Cereal Crop Field Trials with Endothall.								
Sweet Corn								
Sodus, NY 2006 NY$17	1	Sweet corn; Speedy Sweet	K+CWHR	5.0	6.75	0	0.05	NR[3]
			Forage (w/o ears)				0.52	0.65
			Forage (w/ears)				0.49	0.40
			Stover (w/ears)				0.69	0.58
Campbell. MN 2007 MN$10	5	Sweet corn: Vitality	K+CWHR	5.0	6.91	0	0.17	0.17
			Forage (w/o ears)				1.18	1.28
			Forage (w/ears)				0.88	1.06
			Stover (w/ears)				4.70	5.06
Field Corn								
Baptistown, NJ 2006 NJ$18	2	Field corn; TA 3892	Forage	5.0	3.38[4]	0	0.40	0.28
			Grain		6.75		*0.041*[1]	*0.039*[1]
			Stover				3.48	2.89
Sparta, IL 2007 IL$09	5	Field Corn DK61-73	Forage	5.0	6.77	0	0.31	0.34
			Grain				NR[3]	NR[3]
			Stover				1.56	1.39
Richland, IA 2007 IA$06	5	Field Corn 34A16	Forage	5.0	2.26[3]	0	0.35	0.42
			Grain		6.77		NR[3]	NR[3]
			Stover				2.07	2.37
Centerville, SD 2007 SD$05	5	Field Corn DKC 54-46	Forage	5.0	2.40[3]	0	0.36	0.21
			Grain		7.10		NR[3]	NR[3]
			Stover				1.07	1.81
Sorghum								
Sparta, IL 2007 IL$08	5	Sorghum Dekalb 44	Forage	5.0	3.38[4]	0	3.05	2.29
			Grain		6.77		1.41	0.91
			Stover				2.60	7.19
Richland, IA 2007 IA$07	5	Sorghum 85G01	Forage	5.0	3.38[4]	0	0.96	0.57
			Grain		6.77		0.49	0.80
			Stover				1.11	0.81
Larned, KS 2007 KS$03	7	Sorghum Pioneer 87G57	Forage	5.0	2.26[3]	0	0.29	0.41
			Grain		6.77		1.23	1.18
			Stover				3.10	2.65
Wheat								
Ephrata, WA	11	Winter Wheat;	Forage	5.0	2.21[3]	0	0.74	0.63

Residue Data for Endothall								
Trial ID (City, State; Year)	Zone	Crop; Variety	Matrix	Total Rate[4]		PHI (days)	Residues (ppm)[5,6]	
				ppm	lb ae/A			
2007 WA$20		Stevens	Hay				1.00	1.11
			Grain		6.64		0.20	0.25
			Straw				2.20	1.93
Bernard, TX 2007 TX$19	6	Winter wheat; Fannin	Forage	5.0	2.24 [3]	0	1.99	2.27
			Hay				3.09	3.09
			Grain		6.71	1	2.01	1.80
			Straw				2.72	2.76
St, Johns, KS 2007 KS$21	5	Winter Wheat; Jagger	Forage	5.0	2.26 [3]	0	0.84	0.89
			Hay		3.39 [4]		1.31	1.62
			Grain		6.77		0.32	0.32
			Straw				1.49	1.38
Velva, ND 2007 ND$04	7	Spring Wheat; Glenn	Forage	5.0	2.19 [3]	0	0.89	0.94
			Hay		3.29 [4]		2.24	2.09
			Grain		6.58		0.30	0.47
			Straw				1.52	0.61
TABLE C.3.	**Residue Data from Grass Feed Crop Field Trials with Endothall Monoamine Salt (SC/L).**							
Lecompte, LA 2006 LA$12	4	Bermuda grass; Russell	Forage	5.0	7.02	1	2.08	2.23
			Hay				9.80	12.40
East Bernard, TX 2006 TX$14	6	Bermuda grass; Coastal	Forage	5.0	6.75	1	1.85	2.03
			Hay				13.1	14.2
Ephrata, WA 2006 WA$15	11	Bluegrass; Kentucky	Forage	5.0	6.64	1	1.82	1.85
			Hay				7.17	8.91
Newport, SR 2007 AR$37	4	Bluegrass; Kentucky	Forage	5.0	6.76	2	2.65	2.81
			Hay				6.51	6.78
Alexandria, LA 2006 LA$13	4	Fescue; not available	Forage	5.0	7.00	0	1.70	2.86
			Hay				5.89	5.84
Hillsboro, OR 2007 OR$38	12	Fescue; Pure Gold	Forage	5.0	6.73	0	2.65	1.99
			Hay				5.34	9.24
TABLE C.3.	**Residue Data from Non Grass Crop Field Trials with Endothall Monoamine Salt (SC/L).**							
Velva, ND 2007 ND$20	7	Alfalfa; NK919	Forage	5.0	6.58	0	2.13	1.41
			Hay				4.98	4.87
Tilden, IL 2007 IL$30	5	Alfalfa; cattleman's	Forage	5.0	5.94	0	2.24	1.99
			Hay				5.31	3.09
TABLE C.3.	**Residue Data from Crop Field Trials with Endothall Monoamine Salt (SC/L).**							
Velva, ND 2007 ND$20	7	Alfalfa; NK919	Forage	5.0	6.58	0	2.13	1.41
			Hay				4.98	4.87
Tilden, IL 2007 IL$30	5	Alfalfa; cattleman's	Forage	5.0	5.94	0	2.24	1.99
			Hay				5.31	3.09
TABLE C.3.	**Residue Data from Grape Field Trials with Endothall (2 lb ae/gal SC/L).**							
North Rose, NY 2006 NY$01	1	Elvira	Fruit	4.98	6.73	0	0.433	0.376

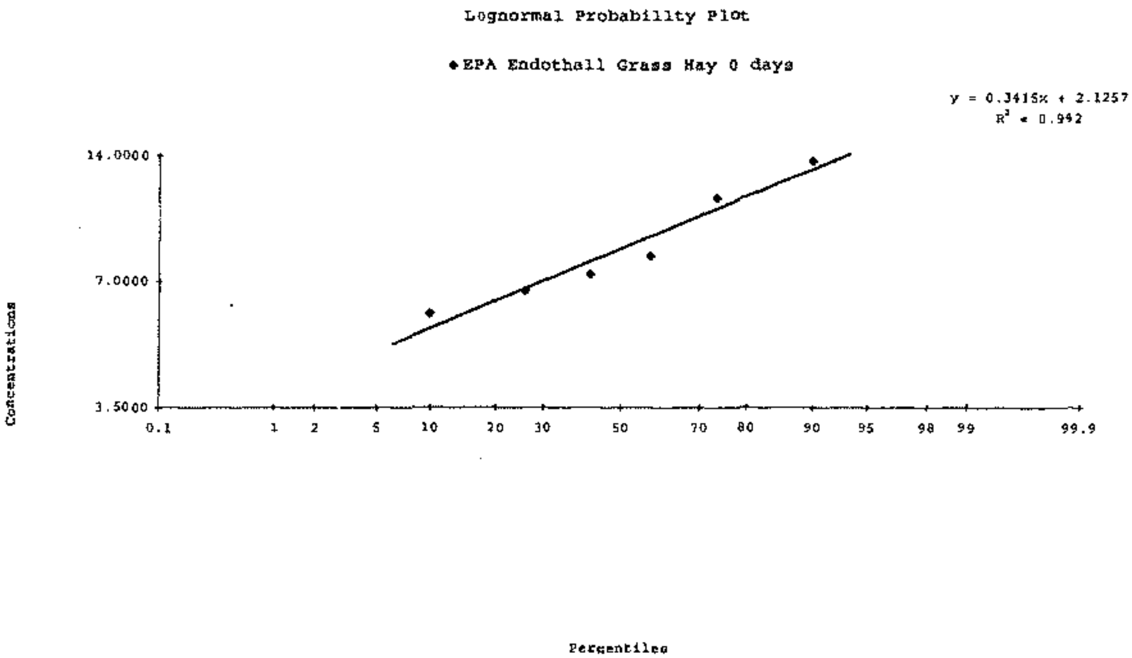
Residue Data for Endothall								
Trial ID (City, State; Year)	Zone	Crop; Variety	Matrix	Total Rate[4]		PHI (days)	Residues (ppm)[5,6]	
				ppm	lb ae/A			
San Luis Obispo, CA 2007 CA$31	10	Pinot 155	Fruit	4.98	6.76	0	0.588	0.449
Ephrata, WA 2006 WA$02	11	Riesling	Fruit	4.97	6.64	0	0.587	0.696
TABLE C.3.	**Residue Data from Rice Field Trials with Endothall Monoamine Salt (SC/L).**							
East Bernard, TX 2007 TX$24	6	Rice; Cocodrie	Grain	5.0	6.75	1	1.22	1.14
			Straw				1.99	2.24
Cheneyville, LA 2007 LA$25	4	Rice; Clearfield 161	Grain	5.0	6.77	0	1.16	1.19
			Straw				1.09	0.94
Newport, AR 2007 AR$26	4	Rice; Wells	Grain	5.0	6.76	0	0.818 [3]	0.694 [3]
			Straw				1.90	1.86
Biggs, CA 2007 CA$27	10	Rice; M-205	Grain	5.0	6.76	0	0.802 [3]	1.08
			Straw				2.59	2.61
TABLE C.3.	**Residue Data from Mint Field Trials with Endothall Monoamine Salt (SC/L).**							
Ephrata, WA 2006 WA$09	11	Mint (Todd's Mitchem)	Tops	5.0	6.64	0	2.89	2.70
Elkhorn, WI 2007 WI$39	5	Mint (Black Mitchem)	Tops	5.0	6.77	0	1.67	1.31

1. Residues below LLMV, but above LOD.
2. Non Detect – no residues seen
3. No Reportable Residues – no residues below the 0.05 ppm LLMV were reported
4. The rate is expressed both in terms of the concentration in the irrigation water (ppm and the total amount (lbs ae/A) applied.
5. Expressed in acid equivalents. The LLMV is 0.05 ppm and the LOD is below 0.001 ppm.
6. The two results for each field trial represent two samples taken from a single plot, not two plots.

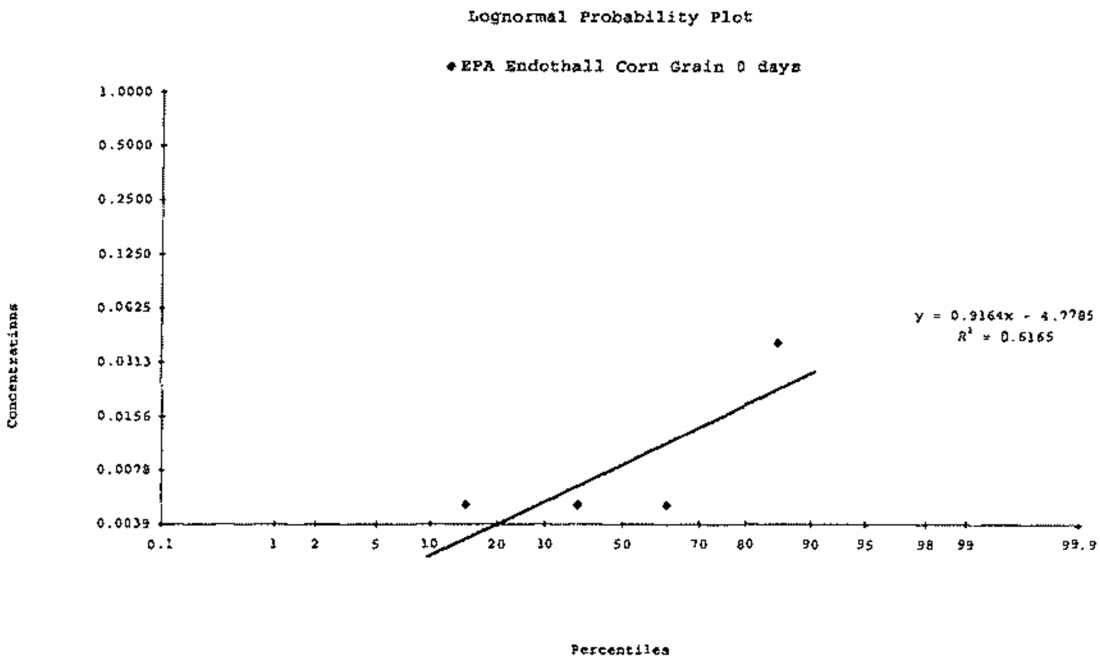
Attachment 2. Tolerance Spreadsheet Results for Crops with Four or More Field Trials – When the Spreadsheet Was Used to Calculate Tolerances (Please note that the spreadsheet was not used when less than four field trials were performed and in those cases where data from multiple crops were combined into a group tolerance.)



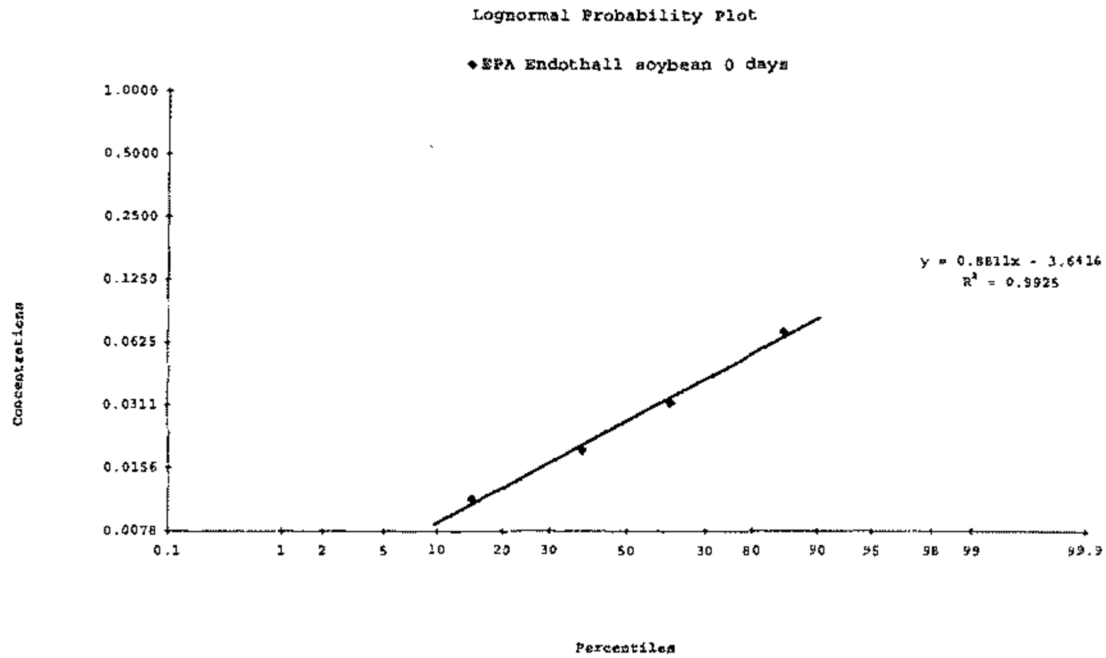
	Regulator: EPA Chemical: Endothall Crop: Grass Forage PHI: 0 days App. Rate: Submitter: n: 6 min: 1.84 max: 2.73 median: 2.22 average: 2.21		
	95th Percentile	99th Percentile	99.9th Percentile
EU Method I Normal	3.0 (3.5)	3.0 (4.0)	3.5 (--)
95/99 Rule	3.0 (4.0)	3.5 (4.5)	3.5 (--)
EU Method II Distribution-Free	#REF!		
Mean+3SD	3.5		
UCLMedian95th	18		
Approximate Shapiro-Francia Normality Test	0.9672 p-value > 0.05 : Do not reject lognormality assumption		



	Regulator: EPA Chemical: Endothall Crop: Grass Hay PHI: 0 days App. Rate: Submitter: n: 6 min: 5.87 max: 13.65 median: 7.67 average: 8.77		
	95th Percentile	**99th Percentile**	**99.9th Percentile**
EU Method I Normal	14 (20)	16 (25)	19 (--)
95/99 Rule	15 (30)	18 (45)	25 (--)
EU Method II Distribution-Free	#REF!		
Mean+3SD	18		
UCLMedian95th	60		
Approximate Shapiro-Francia Normality Test	0.9420 p-value > 0.05 : Do not reject lognormality assumption		



	Regulator: EPA **Chemical:** Endothall **Crop:** Corn Grain **PHI:** 0 days **App. Rate:** **Submitter:** **n:** 4 **min:** 0.01 **max:** 0.04 **median:** 0.01 **average:** 0.01		
	95th Percentile	**99th Percentile**	**99.9th Percentile**
EU Method I Normal	0.05 (0.15)	0.06 (0.15)	0.07 (--)
95/99 Rule	0.05 (1.8)	0.10 (13)	0.25 (--)
EU Method II Distribution-Free	#REF!		
Mean+3SD	0.07		
UCLMedian95th	0.06		
Approximate Shapiro-Francia Normality Test	0.6165 p-value <= 0.01: Reject lognormality assumption		



	Regulator: EPA Chemical: Endothall Crop: soybean PHI: 0 days App. Rate: Submitter: n: 4 min: 0.01 max: 0.07 median: 0.03 average: 0.03		
	95th Percentile	99th Percentile	99.9th Percentile
EU Method I Normal	0.08 (0.20)	0.10 (0.25)	0.15 (--)
95/99 Rule	0.10 (1.6)	0.20 (7.0)	0.30 (--)
EU Method II Distribution-Free	#REF!		
Mean+3SD	0.15		
UCLMedian95th	0.30		
Approximate Shapiro-Francia Normality Test	0.9925 p-value > 0.05 : Do not reject lognormality assumption		

Template Version April 2008

Primary Evaluator	David Soderberg David Soderberg, Chemist, RABV/HED	Date: 5 June 2009
Approved by	William H. Donovan William Donovan, Senior Scientist, RABV, HED	Date: 5 June 2009

This DER was originally prepared under contract by Dynamac Corporation (1910 Sedwick Road, Building 100, Suite B, Durham, NC 27713; submitted 4/07/2009). The DER has been reviewed by the Health Effects Division (HED) and revised as needed for clarity, correctness and to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORT:

47520706. Arsenovic, M. (2008) Endothall (Hydrothol 191): Magnitude of the Residue on Vegetable Fruiting Group: Lab Project Number: Z9766, Z9766.06-CA$28, Z9766.06-FL$27 Unpublished study prepared by Interregional Research Project No. 4. 180 pages.

EXECUTIVE SUMMARY:

Interregional Research Project No. 4 (IR-4) submitted a tomato processing study reflecting the exposure of tomatoes to endothall through the use of treated irrigation water. In a field trial conducted in FL (Zone 3) during 2006, a 2.0 lb ae/gal soluble concentrate (SC/L) formulation of endothall (monoalkylamine salt) was used to treat the irrigation water at a rate of 5 ppm ae. [In order to avoid the complications of different molecular weights for different salts, endothall concentrations are expressed as the free acid equivalents (ae).] The treated water was then applied using overhead sprinklers to tomatoes as six broadcast foliar applications during fruit development at retreatment intervals (RTIs) of 8 days. A volume equivalent to 1 acre inch of water (~27,154 gal/A) was applied for each application. Based on the concentration of the endothall in the irrigation water and the actual amount of water applied, the application rate for endothall was equivalent to 1.13 lb ae/A/application, for a total of 6.77 lb ae/A/season.

Single bulk control and treated samples of tomatoes were harvested at normal crop maturity, immediately following the last irrigation (0 days after treatment, DAT). The tomatoes were processed into puree and paste using simulated commercial procedures. Samples of whole fruits, puree and paste were stored at ≤-10°C for up to 80 days prior to analysis. The sample storage intervals and conditions are supported by the available storage stability data.

Residues of endothall (free acid) in/on tomato fruit, puree and paste were determined using an adequate LC/MS/MS method (Method No. KP-242R1). For this method, residues were extracted with water and then derivatized with heptafluoro-*p*-tolylhydrazine (HFTH) in 50% H_3PO_4. The derivatized residues were cleaned up by partitioning into methyl t-butyl ether (MTBE) and elution through an amine solid phase extraction (SPE) cartridge. Residues were then analyzed by LC/MS/MS using external standards for quantitation. Residues are expressed in endothall acid equivalents. The validated limit of quantitation (LOQ) for endothall in/on

tomatoes and tomato processed fractions is 0.05 ppm, and the estimated limit of detection was 0.002 ppm

Residues of endothall were reported to be <0.05 ppm in/on whole fruits and puree and 0.069 ppm in tomato paste. However, on page 81 it is reported that "The residues of endothall in treated samples ranged from <0.027 to 0.30 ppm. Endothall residues were found less than LOQ in all processed control tomato samples; and 0.021 ppm in whole fruit, 0.069 ppm in tomato paste and 0.044 ppm in tomato puree." From these values, estimated processing factors of 2.1 and 3.3x are calculated here for the puree and paste, respectively. The report only formally estimated the 3.3 factor for paste, but there seems little reason to believe that the 2.1 factor is significantly less supportable than the 3.3 factor, and it provides a factor for the puree that is relatively conservative when compared to EPA's published theoretical factor. EPA's published theoretical processing factors for tomato puree and paste are 1.4 and 5.5x, respectively.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Although the raw data related to the analysis of residues in puree and paste fractions was not included in the study report, the tomato processing residue data are classified as scientifically acceptable under the conditions and parameters used in the study. The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document, DP# 356315.

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported which would have an adverse impact on the validity of the study.

A. BACKGROUND INFORMATION

Endothall [7-oxabicyclo[2,2,1] heptane-2,3-dicarboxylic acid] is a selective contact herbicide, defoliant, desiccant, and aquatic algicide that belongs to the dicarboxylic acid chemical class. The free acid of endothall (PC Code 038901) and its dipotassium (PC Code 038904) and alkylamine (PC Code 038905) salts are registered primarily as aquatic herbicides for the control a variety of plants in water bodies. This includes irrigation canals, but only with a 7 day holding period. They are also registered for desiccation/ defoliation of alfalfa/clover (grown for seed only), cotton, and potatoes prior to harvest, and for reduction of sucker branch growth in hops. Permanent tolerances are established for the combined residues of endothall and its monomethyl ester at 0.1 ppm in/on cotton seeds, fish, dried hops and potatoes, and at 0.05 ppm in/on rice grain and straw [40 CFR §180.293(a)(1)].

In conjunction with a petition for tolerances on a wide variety of irrigated crops (PP# 8E7419), IR-4 has submitted a tomato processing study reflecting irrigation of tomatoes with endothall-treated water. The chemical structure and nomenclature of endothall and its monoalkylamine salt are listed in Table A.1. The physicochemical properties of technical grade endothall and its monoalkylamine salt are listed in Table A.2.

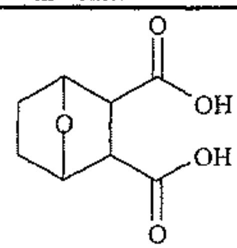
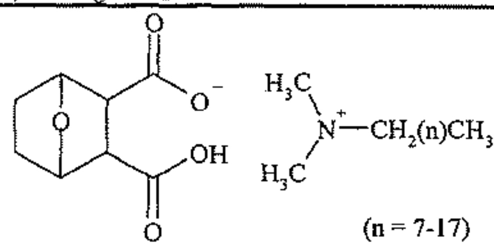
TABLE A.1. Nomenclature of Endothall and its Monoalkylamine Salt.	
Chemical Structure	
Common name	Endothall
Molecular Formula	$C_8H_{10}O_5$
Molecular Weight	186.16
IUPAC name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid
CAS name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid
CAS #	145-73-3
PC Code	038901
Current Food/Feed Site Registration	Cotton, hops, potato, alfalfa grown for seed
Chemical Structure	 (n = 7-17)
Common name	Endothall, mono-N,N-dimethylalkyl amine salt
Molecular Formula	Not available
Molecular Weight	Average: 422
IUPAC name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid, compound with N,N-dimethylcocoamine
CAS name	Not available
CAS #	66330-88-9
PC Code	038905
Current Food/Feed Site Registration	Cotton, hops, potato, alfalfa grown for seed, aquatic uses

TABLE A.2. Physicochemical Properties of Endothall and Its Monoalkylamine Salt.		
Parameter	Value	Reference
Endothall (acid)		
Melting point	108-110℃	D187593, D187590, and D187588, 5/5/93, K. Dockter
pH	2.7 at 25℃ (1% solution)	D187593, D187590, and D187588, 5/5/93, K. Dockter
Density, bulk density, or specific gravity	0.481 g/cm^3 (bulk) at 25℃	D187593, D187590, and D187588, 5/5/93, K. Dockter
Water solubility at 25℃	109.8 g/L 13.1 g/100 mL in water, pH 5 12.7 g/100 mL in water, pH 7 12.5 g/100 mL in water, pH 9	D166798, 7/2/92, K. Dockter D207011, 9/30/94, F. Toghrol
Solvent solubility at 25℃	3.4 g/100 mL in acetonitrile 2.4 g/100 mL in n-octanol 16.0 g/100 mL in tetrahydrofuran	D207011, 9/30/94, F. Toghrol

TABLE A.2. Physicochemical Properties of Endothall and Its Monoalkylamine Salt.		
Parameter	Value	Reference
Vapor pressure	3.92×10^{-5} mm Hg at 24.3°C	D166798, 7/2/92, K. Dockter
Dissociation constant, pK_a	4.32 for Step 1 and 6.22 for Step 2 at 20°C (0.2% solution in 20% basic ethanol); dissociation rate $1.8\text{-}2.3 \times 10^3$ μmho within 3-5 minutes at □25°C, by conductivity meter	D188708, 5/3/93, K. Dockter
Octanol/water partition coefficient	Not applicable to endothall acid	D166798, 7/2/92, K. Dockter
UV/visible absorption spectrum	Not available	
Endothall, mono-N,N-dimethylalkyl amine salt		
Boiling point	Not available	
pH	5.2 at 25°C (1% solution)	D187593, D187590, and D187588, 5/5/93, K. Dockter
Density, bulk density, or specific gravity	1.028 g/mL at 25°C	D187593, D187590, and D187588, 5/5/93, K. Dockter
Water solubility at 25°C	≥49.2 g/100mL in water, pH 5 ≥51.6 g/100 mL in water, pH 7 ≥49.8 g/100 mL in water, pH 9	D210814, 8/9/95, S. Knizner
Solvent solubility at 25°C	≥102.5 g/100mL in acetonitrile ≥95.4 g/100 mL in n-octanol ≥104.3 g/100 mL in tetrahydrofuran	D210814, 8/9/95, S. Knizner
Vapor pressure	2.09×10^{-5} mm Hg at 25°C (calculated; mixed mono- and dialkylamine (C8-C20))	D206344, 9/22/94, F. Toghrol
Dissociation constant, pK_a	4.24 for Step 1 and 6.07 for Step 2 at 20°C for mixed mono- and dialkylamine (C8-C20) in acidified ethanol/water; dissociation complete □17 minutes (1.7×10^3 μmho) at 25°C	D198885, 4/7/94, F. Toghrol
Octanol/water partition coefficient	K_{OW} 2.097 at concentrations of 8.9×10^{-3} M and 8.9×10^{-4} M, at 25°C	D209995, 1/20/95, L. Edwards
UV/visible absorption spectrum	Not available	

B. EXPERIMENTAL DESIGN

B.1. Application and Crop Information

In a field trial conducted in FL (Zone 3) during 2006, tomatoes were irrigated with endothall-treated water using overhead sprinklers (Table B.1.1). The irrigation water was treated with endothall (2.0 lb ae/gal SC/L monoalkylamine salt) at a concentration of ~5 ppm, acid equivalent. The tomatoes were irrigated six times during flowering and fruit development at RTIs of 8 days. A volume equivalent to ~1 acre inch of water (27,154 gal/A) was applied for each irrigation. Based on the concentration of the endothall and the actual amount of water applied, application rate for endothall was equivalent to 1.13 lb ae/A/application, for a total of 6.77 lb ae/A/season.

TABLE B.1.1. Study Use Pattern.							
Location (City, State; Year) Trial ID	End-Use Product	Application Information					
		Method; Timing	Concen. [1]	Volume (gal/A) [2]	Single Rate (lb ae/A) [3]	RTI [4] (days)	Total Rate (lb ae/A) [3]
Oviedo, FL 2006 FL$27	2.0 lb/gal SC/L	Six broadcast foliar application during flowering and fruit development using overhead sprinklers.	5.0	27,160-27,165	1.13	8	6.77

[1] The concentrate of endothall (in acid equivalents) in the irrigation water. No adjuvants were included in the irrigation water.
[2] The target irrigation rate was 1 acre inch of water or 27,154 gal/A.
[3] The equivalent field use rates were calculated by the reviewer based on the concentration of the endothall (ae), the application volume and plot size.
[4] RTI = Retreatment Interval.

B.2. Sample Handling and Processing Procedures

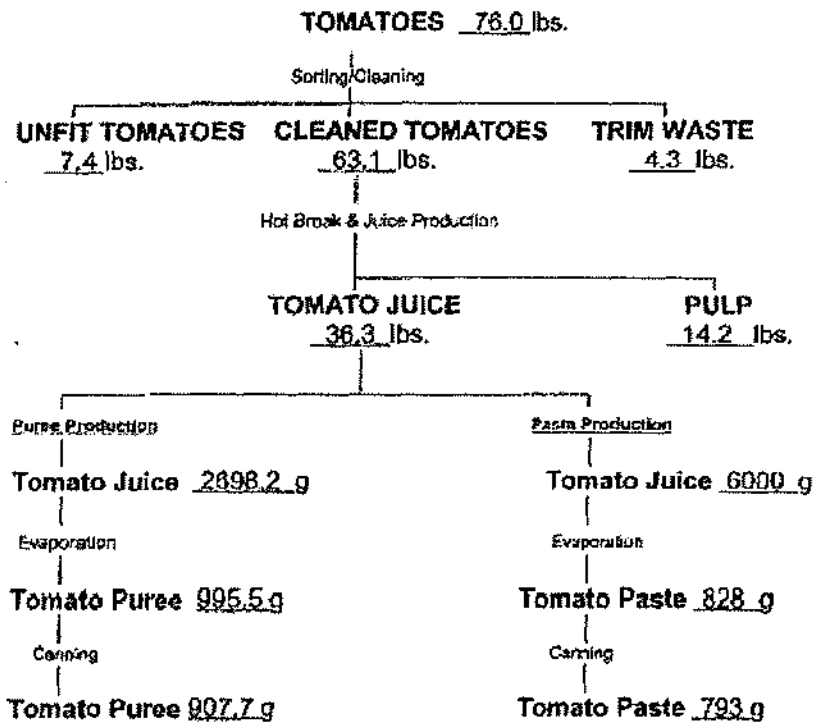
Single bulk control and treated samples of mature tomatoes (85-95 lb/sample) were harvested at 0 DAT and shipped the same day under ambient conditions by overnight courier to the processing facility, GLP Technologies (Navasota, TX). The samples were held in cool storage 4 ± 3°C for 6 days until processing.

The tomato samples were processed according to simulated commercial procedures into puree and paste (Figure B.1). A subsample of whole fruits was collected prior to processing, and the bulk whole fruit samples were then cleaned and rinsed in hot water. The fruit was next chopped to a fine consistency, heated to 91-97°C, and passed through a pulper/finisher to yield pulp and juice fractions. The juice was adjusted to an acidity of pH ≤4.6 if necessary and then concentrated under heat and vacuum to 8-24% solids for puree and 24-30% solids for paste. Samples of puree and paste were collected and stored at ≤-10°C. Processing was completed within 11days of harvest.

Within 3 days of processing, the subsamples for whole fruits and each processed fraction were shipped frozen (on dry ice) by overnight courier to the analytical laboratory, Cerexagri, Inc., (King of Prussia, Pennsylvania). At the analytical laboratory, the samples were stored frozen (≤-18°C) prior to analysis.

FIGURE B.1. Processing Flowchart for Tomato.

Sample # 2 (TREATED) Code # F (Treatment 02)



B.3. Analytical Methodology

Residues of endothall (free acid) in/on tomato fruit, puree and paste were determined using a LC/MS/MS method (Method No. KP-242R1) entitled "Analytical Method for Determination of Endothall in Crops", issued 5/4/2007.

For this method, residues were extracted twice by homogenization with water followed by centrifugation and filtering. Residues were then derivatized with HFTH in 50% H_3PO_4 at 100-120°C for 90 minutes. After cooling, the derivatized residues were partitioned into MTBE, evaporated to dryness, and reconstituted in hexane:MTBE (1:1 v:v). Residues were then cleaned using an amine SPE cartridge eluted with methanol:MTBE (1:4). Residues were analyzed by LC/MS/MS using external standards. The m/z 397→166 ion transition was used for quantifying residues. Residues are expressed in endothall acid equivalents. The validated LOQ for endothall in/on tomato fruits, puree and paste is 0.05 ppm, and the LOD was estimated to be 0.002 ppm.

Control samples of tomatoes were fortified with endothall at 0.05-5.0 ppm for method validation. For concurrent recoveries, control samples were fortified with endothall at 0.05 and 0.5 ppm for whole fruits and at 0.05 and 2.0 ppm for paste.

C. RESULTS AND DISCUSSION

The LC/MS/MS method used for determining residues of endothall in/on tomato fruit, puree, and paste was adequately validated prior to and in conjunction with the analysis of processing study samples. Method validation recoveries averaged 89% with a standard deviation of 7% for whole tomatoes (Table C.1). Concurrent recoveries averaged 101 and 86% for whole tomatoes and tomato paste, respectively. Apparent residues of endothall were <LOQ in/on all control samples. Adequate sample calculations and example chromatograms were provided and the fortification levels used for method recoveries were similar in magnitude to the measured residue levels.

Samples of tomato fruits, puree and paste were stored frozen at ≤-5°C for up to 80 days prior to analysis (Table C.2). Adequate storage stability data are available indicating that endothall is stable under frozen storage conditions for up to 467 days in whole tomatoes (47520719.der, under review). These stability data will support the storage durations and conditions for the tomato processing study.

Following six overhead sprinkler applications of endothall (monoalkylamine salt) to tomatoes at rates totaling 6.77 lb ae/A, residues in/on whole fruits were 0.021 ppm at 0 DAT (Table C.3). Residues in processed tomato puree and paste were <0.05 ppm and 0.069 ppm, respectively. Although the report listed residues in whole fruit and puree as being <0.05 ppm, the raw data contained information showing that residues were detectable in/on whole fruits; however, the raw data for the puree fraction was not included in the report. The processing factor was 3.3x for paste; however, the processing factor for puree could not be calculated. The theoretical processing factors for tomato juice, puree and paste are 1.4x, 1.4x and 5.5x, respectively.

TABLE C.1. Summary of Method Validation and Concurrent Recoveries of Endothall from Tomato Fruits and Paste.

Matrix	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean ± Std. Dev. [1] (%)
Method Validation				
Tomato fruit	0.05	3	82, 79, 84	82 ± 3
	0.5	3	100, 92, 97	96 ± 4
	5.0	3	86, 93, 92	90 ± 4
	Total	9	79-100	89 ± 7
Concurrent Recoveries				
Tomato fruit	0.05	1	104	101
	0.5	1	98	
Tomato paste	0.05	0.05	92	86
	1.0	2.0	80	

[1] Standard deviations are calculated for data sets having ≥3 values.

TABLE C.2. Summary of Storage Conditions.

Matrix	Storage Temperature (°C)	Actual Storage Duration (days)[1]	Interval of Demonstrated Storage Stability (days)[2]
Whole tomatoes	≤-5	77-80	467
Puree and paste		80	

[1] Interval from harvest to extraction for analysis. Samples were extracted up to 1 day prior to analysis.
[2] Endothall is stable under frozen storage conditions for up to 467 days in tomatoes (47520719.der under review).

TABLE C.3. Residue Data from Tomato Processing Study with Endothall Monoalkylamine Salt (SC/L).

RAC	Processed Commodity	Total Rate [1]		PHI (days)	Residues (ppm) [2]	Processing Factor
		ppm	lb ae/A			
Tomato	Whole fruit (RAC)	5.0	6.64	0	0.021 [3]	--
	Puree				0.044 [4]	2.1x[4]
	Paste				0.069	3.3x

[1] The rate is expressed both in terms of the concentration in the irrigation water (ppm) and the total amount (lb ae/A) applied.
[2] Expressed in acid equivalents. The LOQ is 0.05 ppm and the estimated LOD is 0.002 ppm.
[3] Although reported as <LOQ, detectable endothall residues (≥LOD) were reported in the raw data (page 64).
[4] Raw residue data were not formally reported for the puree sample; however, on page 81 residue values below the LLMV, but above the LOD are provided as 0.021 in raw fruit, 0.044 ppm in puree, 0.069 in paste. The values of 0.021 and 0.069 are formally considered acceptable. There seems little reason to reject the 0.044 ppm value when it provides a processing factor that is somewhat conservative relative to the theoretical factor, and makes reasonable sense given the mass balance estimates.

D. CONCLUSION

The tomato processing study is adequate. Endothall residues appear roughly to concentrate by 2.1x in tomato puree, and by 3.3x in tomato paste, however both factors are based upon values that are all below the LLMV of the method.

E. REFERENCES

None

F. DOCUMENT TRACKING

RDI: David Soderberg (5 June 2009); William Donovan (5 June 2009)
Petition Number: 8E7419
DP#: 356315
PC Code: 038901 and 038905

Template Version June 2005

Primary Evaluator	David Soderberg, Chemist, RABV, HED	Date: 5 June 2009
Approved by	William Donovan, Senior Scientist, RABV, HED	Date: 5 June 2009

This DER was originally prepared under contract by Dynamac Corporation (1910 Sedwick Road, Building 100, Suite B, Durham, NC 27713; submitted 3/27/2009). The DER has been reviewed by the Health Effects Division (HED) and revised as needed for clarity, correctness and to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORT:

47520708. Arsenovic, M. (2008) Endothall (Hydrothol 191): Magnitude of the Residue on Fruit, Citrus Group: Lab Project Number: Z9759, Z9759.07-CER08 Unpublished study prepared by Interregional Research Project No. 4. 230 pages.

EXECUTIVE SUMMARY:

Interregional Research Project No. 4 (IR-4) submitted field trial data reflecting the exposure of oranges to endothall through the use of treated irrigation water. In two orange field trials conducted during 2006 in Zones 3 and 10, a 2.0 lb ae/gal soluble concentrate (SC/L) formulation of endothall (monoalkylamine salt) was used to treat the irrigation water at a rate of 5 ppm ae. [In order to avoid the complications of different molecular weights for different salts, endothall concentrations are expressed as the free acid equivalents (ae).] The treated water was applied to the orange trees during fruit development as six broadcast foliar applications using overhead sprinklers, at retreatment intervals (RTIs) of 5-8 days. A volume equivalent to ~1 acre inch of water (27,154 gal/A) was applied for each application. Based on the concentration of the endothall and the amount of water applied, the application rates for endothall were equivalent to 1.10-1.13 lb ae/A/application, for a total of 6.63-6.78 lb ae/A/season.

Single control and duplicate treated samples of oranges were harvested from each test on the day of the final application (0 days after treatment, DAT), and samples were stored at ≤-18°C for up to 107 days prior to analysis. Adequate storage stability data are available to support the duration and conditions of sample storage.

Residues of endothall (free acid) in/on oranges were determined using an adequate LC/MS/MS method (Method No. KP-242R1). For this method, residues were extracted with water and then derivatized with heptafluoro-*p*-tolylhydrazine (HFTH) in 50% H_3PO_4. The derivatized residues were cleaned up by partitioning into methyl t-butyl ether (MTBE) and elution through an amine solid phase extraction (SPE) cartridge. Residues were then analyzed by LC/MS/MS using external standards for quantitation. Residues are expressed in endothall acid equivalents. The validated limit of quantitation (LOQ) for endothall in/on oranges is 0.05 ppm, and the estimated limit of detection was 0.0025 ppm.

Following six overhead sprinkler applications with irrigation water containing endothall at 5 ppm (6.63-6.78 lb ae/A/season), endothall residues were <LOQ in/on four orange samples at 0 DAT. However, detectable residues were found on all four samples at 0.021-0.028 ppm. The average and highest average field trial (HAFT) residues were <0.05 ppm in/on oranges.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the orange field trial residue data are scientifically acceptable. Although limited field trials were performed, these applications are expected to be conservative relative to actual inadvertent applications. The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document [DP# 356315].

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported which would have an adverse impact on the validity of the study.

A. BACKGROUND INFORMATION

Endothall [7-oxabicyclo[2,2,1] heptane-2,3-dicarboxylic acid] is a selective contact herbicide, defoliant, desiccant, and aquatic algicide that belongs to the dicarboxylic acid chemical class. The free acid of endothall (PC Code 038901) and its dipotassium (PC Code 038904) and alkylamine (PC Code 038905) salts are registered primarily as aquatic herbicides for the control a variety of plants in water bodies. This includes irrigation canals, but only with a 7 day holding period. They are also registered for desiccation/ defoliation of alfalfa/clover (grown for seed only), cotton, and potatoes prior to harvest, and for reduction of sucker branch growth in hops. Permanent tolerances are established for the combined residues of endothall and its monomethyl ester at 0.1 ppm in/on cotton seeds, fish, dried hops and potatoes, and at 0.05 ppm in/on rice grain and straw [40 CFR §180.293(a)(1)].

In conjunction with a petition for tolerances on a wide variety of irrigated crops (PP# 8E7419), IR-4 has submitted field trial data reflecting irrigation of oranges with endothall-treated water. The chemical structure and nomenclature of endothall and its monoalkylamine salt are listed in Table A.1. The physicochemical properties of technical grade endothall and its monoalkylamine salt are listed in Table A.2.

Table A.1. Nomenclature of Endothall and its Monoalkylamine Salt.

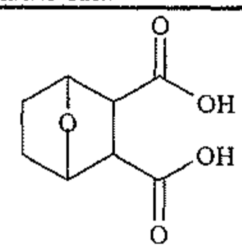
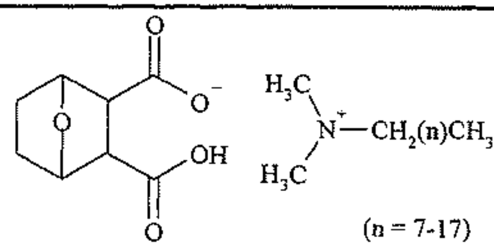
Chemical Structure	
Common name	Endothall
Molecular Formula	$C_8H_{10}O_5$
Molecular Weight	186.16
IUPAC name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid
CAS name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid
CAS #	145-73-3
PC Code	038901
Current Food/Feed Site Registration	Cotton, hops, potato, alfalfa grown for seed
Chemical Structure	 (n = 7-17)
Common name	Endothall, mono-N,N-dimethylalkyl amine salt
Molecular Formula	Not available
Molecular Weight	Average: 422
IUPAC name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid, compound with N,N-dimethylcocoamine
CAS name	Not available
CAS #	66330-88-9
PC Code	038905
Current Food/Feed Site Registration	Cotton, hops, potato, alfalfa grown for seed, aquatic uses

Table A.2. Physicochemical Properties of Endothall and Its Monoalkylamine Salt.

Parameter	Value	Reference
Endothall (acid)		
Melting point	108-110°C	D187593, D187590, and D187588, 5/5/93, K. Dockter
pH	2.7 at 25°C (1% solution)	D187593, D187590, and D187588, 5/5/93, K. Dockter
Density, bulk density, or specific gravity	0.481 g/cm^3 (bulk) at 25°C	D187593, D187590, and D187588, 5/5/93, K. Dockter
Water solubility at 25°C	109.8 g/L 13.1 g/100 mL in water, pH 5 12.7 g/100 mL in water, pH 7 12.5 g/100 mL in water, pH 9	D166798, 7/2/92, K. Dockter D207011, 9/30/94, F. Toghrol
Solvent solubility at 25°C	3.4 g/100 mL in acetonitrile 2.4 g/100 mL in n-octanol 16.0 g/100 mL in tetrahydrofuran	D207011, 9/30/94, F. Toghrol
Vapor pressure	3.92×10^{-5} mm Hg at 24.3°C	D166798, 7/2/92, K. Dockter

Table A.2. Physicochemical Properties of Endothall and Its Monoalkylamine Salt.

Parameter	Value	Reference
Dissociation constant, pK_a	4.32 for Step 1 and 6.22 for Step 2 at 20℃ (0.2% solution in 20% basic ethanol); dissociation rate 1.8-2.3 x 10^3 µmho within 3-5 minutes at □25℃, by conductivity meter	D188708, 5/3/93, K. Dockter
Octanol/water partition coefficient	Not applicable to endothall acid	D166798, 7/2/92, K. Dockter
UV/visible absorption spectrum	Not available	
Endothall, mono-N,N-dimethylalkyl amine salt		
Boiling point	Not available	
pH	5.2 at 25℃ (1% solution)	D187593, D187590, and D187588, 5/5/93, K. Dockter
Density, bulk density, or specific gravity	1.028 g/mL at 25℃	D187593, D187590, and D187588, 5/5/93, K. Dockter
Water solubility at 25℃	≥49.2 g/100mL in water, pH 5 ≥51.6 g/100 mL in water, pH 7 ≥49.8 g/100 mL in water, pH 9	D210814, 8/9/95, S. Knizner
Solvent solubility at 25℃	≥102.5 g/100mL in acetonitrile ≥95.4 g/100 mL in n-octanol ≥104.3 g/100 mL in tetrahydrofuran	D210814, 8/9/95, S. Knizner
Vapor pressure	2.09 x 10^{-5} mm Hg at 25℃ (calculated; mixed mono- and dialkylamine (C8-C20))	D206344, 9/22/94, F. Toghrol
Dissociation constant, pK_a	4.24 for Step 1 and 6.07 for Step 2 at 20℃ for mixed mono- and dialkylamine (C8-C20) in acidified ethanol/water; dissociation complete □17 minutes (1.7 x 10^3 µmho) at 25℃	D198885, 4/7/94, F. Toghrol
Octanol/water partition coefficient	K_{OW} 2.097 at concentrations of 8.9 x 10^{-3} M and 8.9 x 10^{-4} M, at 25℃	D209995, 1/20/95, L. Edwards
UV/visible absorption spectrum	Not available	

B. EXPERIMENTAL DESIGN

B.1. Study Site Information

Two orange field trials were conducted in Zones 3 and 10 during 2006 (Table B.1.1). The irrigation water used in each test was treated with endothall (2.0 lb ae/gal SC monoalkylamine salt) at a concentration of ~5 ppm, acid equivalent. The treated water was applied to the orange trees during fruit development as six broadcast foliar applications using overhead sprinklers, at RTIs of 5-8 days. A volume equivalent to ~1 acre inch of water (~27,154 gal/A) was applied for each application. Based on the concentration of the endothall and the amount of water applied, application rates for endothall were equivalent to 1.10-1.13 lb ae/A/application, for a total of 6.63-6.78 lb ae/A/season (Table B.1.3). These applications are expected to be conservative relative to actual applications.

TABLE B.1.1. Trial Site Conditions.				
Trial Identification (City, State; Year)	Soil characteristics[1]			
	Type	%OM	pH	CEC (meq/100g)
Dinuba, CA 2006 CA$11	Sandy Loam	1.4	5.1	13.8
Oviedo, FL 2006 FL$10	Sand	1.1	5.3	2.8

[1]These parameters are optional except in cases where their value affects the use pattern for the chemical.

TABLE B.1.2. Water Characterization.					
Study site	Water characteristics				
	Type	Hardness/Salinity	pH	Turbidity	Dissolved OM
Dinuba, CA 2006 CA$11	Well	NR	NR	NR	NR
Oviedo, FL 2006 FL$10	Artesian Well	NR	NR	NR	NR

NR = Not reported.

The actual temperature recordings and rainfall were typical for each site and no unusual weather conditions were reported. No additional irrigation was reported during the study period. The tests were conducted according to normal agricultural practices for the regions, and information was provided on maintenance pesticides and fertilizers used at each site. No information was provided on the characteristics of the water used for irrigation, other than the source (Table B.1.2).

TABLE B.1.3. Study Use Pattern.							
Location (City, State; Year) Trial ID	End-Use Product	Application Information					
		Method; Timing	Concen. [1]	Volume (gal/A) [2]	Single Rate (lb ae/A) [3]	RTI [4] (days)	Total Rate (lb ae/A) [3]
Dinuba, CA 2006 CA$11	2.0 lb/gal SC	Six broadcast foliar application during fruit development using overhead sprinklers.	5.0	27,150	1.13	7-8	6.78
Oviedo, FL 2006 FL$10	2.0 lb/gal SC	Six broadcast foliar application during fruit development using overhead sprinklers.	5.0	26,701-26,721	1.10	5-6	6.63

[1] The concentration of endothall (in acid equivalents) in the irrigation water. No adjuvants were included in the irrigation water.
[2] The target irrigation rate was 1 acre inch of water or 27,154 gal/A.
[3] The equivalent field use rates were calculated by the reviewer based on the concentration of the endothall (ae), the application volume and plot size.
[4] RTI = Retreatment Interval.

TABLE B.1.4. Trial Numbers and Geographical Locations.

NAFTA Growing Zones [2]	Orange		
	Submitted	Requested[1]	
		Canada	U.S.
1	--	--	--
2	--	--	--
3	1	--	8
4	--	--	--
5	--	--	--
6	--	--	1
7	--	--	--
8	--	--	--
9	--	--	--
10	1	--	3
11	--	--	--
12	--	--	--
13	--	--	--
Total	2	--	12

[1] Based on EPA OPPTS Guideline 860.1500.
[2] Zones 1A, 5 A and B, 7A and 14-21 were not included as the proposed use is for the U.S. only.

B.2. Sample Handling and Preparation

Duplicate control and treated samples (≥8.5 lb sample, 24 fruits) of oranges were harvested at 0 DAT (after the sixth application) and placed in frozen storage at the test facility within 6 hours. Samples were stored frozen at the field sites for 0-34 days prior to shipment by ACDS Freezer truck to the analytical laboratory, Cerexagri, Inc. (King of Prussia, PA), where the samples were stored at ≤-18°C until analysis.

B.3. Analytical Methodology

Residues of endothall (free acid) in/on oranges were determined using a LC/MS/MS method (Method No. KP-242R1) entitled "Analytical Method for Determination of Endothall in Crops", issued 5/4/2007.

For this method, residues were extracted twice by homogenization with water followed by centrifugation and filtering. Residues were then derivatized with HFTH in 50% H_3PO_4 at 100-120°C for 90 minutes. After cooling, the derivatized residues were partitioned into MTBE, evaporated to dryness, and reconstituted in hexane:MTBE (1:1 v:v). Residues were then cleaned using an amine SPE cartridge eluted with methanol:MTBE (1:4). Residues were analyzed by LC/MS/MS using external standards. The m/z 397→166 ion transition was used for quantifying residues. Residues are expressed in endothall acid equivalents. The validated LOQ for endothall in/on oranges is 0.05 ppm, and the LOD was estimated to be 0.0025 ppm.

The above method was validated prior to and in conjunction with the analysis of the field trial samples. Control samples of oranges were fortified with endothall at 0.05-5.0 ppm for method validation, and control samples were fortified with endothall at 0.05-1.0 ppm for concurrent recoveries.

C. RESULTS AND DISCUSSION

The LC/MS/MS method used for determining residues of endothall in/on oranges was adequately validated prior to and in conjunction with the analysis of field trial samples. Method validation recovery averaged 75% with a standard deviation of 4%, and concurrent recoveries averaged 73% with a standard deviation of 2% (Table C.1). Apparent residues of endothall were <LOD in/on all control samples. Adequate sample calculations and example chromatograms were provided and the fortification levels used for method recoveries were similar in magnitude to the measured residue levels.

Orange samples were stored frozen at ≤-18°C for up to 107 days prior to analysis. Adequate storage stability data are available indicating that endothall is stable in frozen tomatoes for up to 467 days (47520719.der, under review). These data will support the storage durations and conditions for the current field trials.

Following six overhead sprinkler applications with irrigation water containing endothall at 5 ppm (6.63-6.78 lb ae/A/season), endothall residues at 0 DAT were <LOQ in/on four orange samples; however, detectable residues were found on all four samples at 0.021-0.028 ppm (Table C.3). The average and HAFT residues were 0.05 ppm in/on oranges (Table C.4).

No phytotoxicity was reported on the treated trees. Common cultural practices were used to maintain plants, and the weather conditions and maintenance chemicals and fertilizer used in this study did not have a notable impact on the residue data.

TABLE C.1. Summary of Method Validation and Concurrent Recoveries of Endothall from Oranges.

Matrix	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean ± Std. Dev. (%)
Method Validation				
Fruit	0.05	3	76, 72, 74	74 ± 2
	0.5	3	72, 72, 73	72 ± 1
	5.0	3	76, 73, 85	78 ± 6
	Total	**9**	**72-85**	**75 ± 4**
Concurrent Recoveries				
Fruit	0.05	2	76, 71	74
	0.5	1	74	74
	1.0	1	72	72
	Total	**4**	**71-76**	**73 ± 2**

[1] Standard deviations are calculated for data sets having ≥3 values.

TABLE C.2. Summary of Storage Conditions.

Matrix	Storage Temperature (°C)	Actual Storage Duration (days)[1]	Interval of Demonstrated Storage Stability (days)[2]
Orange fruit	≤-18	105-107	467

[1] Interval from harvest to extraction for analysis. Extracts were stored up to 2 days prior to analysis.
[2] Endothall is stable in frozen tomatoes for up to 467 days (47520719.der under review).

TABLE C.3. Residue Data from Orange Field Trials with Endothall Monoalkylamine Salt (SC/L).

Trial ID (City, State; Year)	Zone	Variety	Matrix	Total Rate[1]		PHI (days)	Residues (ppm)[2,3]	
				ppm	lb ae/A			
Dinuba, CA 2006 CA$11	10	Rush Thompson Improved	Fruit	5.0	6.78	0	(0.024)	(0.028)
Oviedo, FL 2006 FL$10	3	Hamlin	Fruit	5.0	6.63	0	(0.022)	(0.021)

[1] The rate is expressed both in terms of the concentration in the irrigation water (ppm) and the total amount (lb ae/A) applied.
[2] Expressed in acid equivalents. The LOQ is 0.05 ppm and the LOD was estimated to be 0.0025 ppm. Values <LOQ but ≥LOD are listed in parentheses.
[3] The two results for each field trial represent two samples taken from a single plot, not two plots.

TABLE C.4. Summary of Residue Data from Orange Field Trials with Endothall Monoalkylamine Salt (SC/L).

Commodity	Total Applic. Rate[1]	PHI (days)	Residue Levels (ppm)[2]						
			N	Min.	Max.	HAFT[3]	Median (STMdR)	Mean (STMR)	Std. Dev.
Orange	5 ppm (6.63-6.78)	0	2	0.0215	0.026	0.026	0.024	0.024	0.0032

[1] The value in parentheses is the total application rate in terms of lb ae/A.
[2] Residues are expressed in terms of the free acid. The LOQ is 0.05 ppm. For all values reported ≤LOQ, the LOQ was used for all calculations.
[3] HAFT = Highest Average Field Trial.

D. CONCLUSION

The available field trial data are adequate and support the use of endothall-treated water for irrigation of citrus trees. The data support the use of endothall in irrigation water at a concentration of 5 ppm (ae), with no more that six applications per season and a minimum 7-day interval between applications to the water. Residues in oranges are determined at a 0-day PHI.

E. REFERENCES

None

F. DOCUMENT TRACKING

RDI: David Soderberg (5 June 2009); William Donovan (5 June 2009)
Petition Number: 8E7419
DP#: 356315
PC Codes: 038901 and 038905

Template Version June 2005

Primary Evaluator	David Soderberg, Chemist, RABV/HED	Date: 5 June 2009
Approved by	William Donovan, Senior Scientist, RABV, HED	Date: 5 June 2009

This DER was originally prepared under contract by Dynamac Corporation (1910 Sedwick Road, Building 100, Suite B, Durham, NC 27713; submitted 3/25/2009). The DER has been reviewed by the Health Effects Division (HED) and revised as necessary for clarity, correctness or to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORT:

47520701. Arsenovic, M. (2008) Endothall (Hydrothol 191 and Aquathol K): Magnitude of the Residue on Vegetable, Root and Tuber Group: Lab Project Number: Z9762. Unpublished study prepared by Interregional Research Project No. 4. 389 pages.

EXECUTIVE SUMMARY:

Interregional Research Project No. 4 (IR-4) submitted field trial data reflecting the exposure of representative root and tuber vegetables to endothall through the use of treated irrigation water. Two field trials each were conducted on sugar beets, carrots, and potatoes in Zones 5, 10 and 11 during 2006-2007. In each test, a 2.0 lb ae/gal soluble concentrate (SC/L) formulation of endothall (monoalkylamine salt) was used to treat the irrigation water at a rate of 5 ppm ae. [In order to avoid the complications of different molecular weights for the different salts, endothall concentrations are expressed as the free acid equivalents (ae).] In addition, in the two sugar beet field trials, side-by-side test were also conducted using the dipotassium salt of endothall applied to the irrigation water at a concentration of 3.5 ppm ae. The treated water was applied during vegetative development as six broadcast foliar applications using overhead sprinklers, at retreatment intervals (RTIs) of 6-8 days. A volume equivalent to ~1 acre inch of water (27,154 gal/A) was applied for each application. Based on the concentration of the endothall and the amount of water applied, the application rates for the monoalkylamine salt of endothall were equivalent to 1.13-1.14 lb ae/A/application, for a total of 6.77-6.83 lb ae/A/season (Table B.1.3). The application rates for the dipotassium salt were equivalent to 0.80-0.81 Ib ae/A/application, for a total of 4.80-4.88 lb ae/A/season.

Single control and duplicate treated samples of sugar beet roots and tops, carrot roots and potatu tubers were harvested from the respective tests on the day of the final application (0 days after treatment, DAT). Carrot, potato, and sugar beet samples were stored at <-18°C for up to 272, 58, and 64 days, respectively, prior to analysis. These sample storage intervals are supported by the available storage stability data.

Residues of endothall (free acid) were determined using an adequate LC/MS/MS method (Method No. KP-242R1). For this method, residues were extracted with water and then derivatized with heptafluoro-*p*-tolylhydrazine (HFTH) in 50% H_3PO_4. The derivatized residues were cleaned up by partitioning into methyl t-butyl ether (MTBE) and elution through an amine solid phase extraction (SPE) cartridge. Residues were then analyzed by LC/MS/MS using external standards for quantitation. Residues are also expressed in endothall acid equivalents. The validated limit of quantitation (LOQ) for endothall in/on onions is 0.05 ppm, expressed in acid equivalents.

Following six overhead sprinkler applications with irrigation water containing the monoalkylamine salt of endothall at 5 ppm ae (6.77-6.83 lb ae/A/season), endothall residues at 0 DAT were 1.11-1.62 ppm in/on 4 samples of sugar beet tops, 0.136-0.591 ppm in/on 4 samples of sugar beet roots, 0.062-0.088 ppm in/on 4 samples of carrot roots, and 0.067-0.103 ppm in/on 4 samples of potato tubers. Average endothall residues were 1.34 ppm for sugar beet tops, 0.330 ppm for sugar beet roots, 0.078 ppm for carrot roots, and 0.080 ppm for potato tubers. The highest average field trial (HAFT) residues were 1.37 ppm for sugar beet tops, 0.493 ppm for sugar beet roots and 0.088 ppm for both carrot roots and potato tubers. No residue decline data were provided.

Following six overhead sprinkler applications with irrigation water containing the dipotassium salt of endothall at 3.5 ppm ae (4.80-4.88 lb ae/A/season), endothall residues at 0 DAT were 0.523-1.28 ppm in/on 4 samples of sugar beet tops and 0.115-0.345 ppm in/on 4 samples of sugar beet roots. Average endothall residues were 0.821 ppm in/on sugar beet tops and 0.224 ppm in/on sugar beet roots, and HAFT residues in/on sugar beet tops and roots were 1.11 and 0.331 ppm, respectively.

Although average endothall residues in/on sugar beet tops and roots were clearly lower (0.6-0.7x) for the dipotassium salt formulation than for the monoalkylamine salt formulation, direct comparison of the two formulations is not possible because the two formulations were applied at different rates. The monoalkylamine salt was applied at 5 ppm ae, whereas the dipotassium salt was applied at 5.0 ppm, <u>as the salt</u>, which is 3.5 ppm ae, that is, the dipotassium salt is applied at 0.7x the rate of the monoalkylamine salt. [Note that these two different application rates are each entirely consistent with different label directions for the two salts. The two labels specify recipes that lead to application of the dipotasium salt at 5 ppm as the salt, and application of the alkylamine salt as 5 ppm as the free acid.]

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the field trial residue data for the monoalkylamine salt of endothall are scientifically acceptable. However, as explained above, the field trial data for the dipotassium salt were not appropriate for direct comparison with the monoalkylamine salt because the dipotassium was applied at 0.7x the rate of the monoalkylamine salt. Although only very limited field trials, with a single plot each, were performed for each crop, the trials were performed to be conservative relative to actual likely inadvertent treatments of these crops with endothall. The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document, DP# 356315.

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported which would have an adverse impact on the validity of the study.

A. BACKGROUND INFORMATION

Endothall [7-oxabicyclo[2,2,1] heptane-2,3-dicarboxylic acid] is a selective contact herbicide, defoliant, desiccant, and aquatic algicide that belongs to the dicarboxylic acid chemical class. The free acid of endothall (PC Code 038901) and its dipotassium (PC Code 038904) and alkylamine (PC Code 038905) salts are registered primarily as aquatic herbicides for the control a variety of plants in water bodies. This includes irrigation canals, but only with a 7 day holding period. They are also registered for desiccation/ defoliation of alfalfa/clover (grown for seed only), cotton, and potatoes prior to harvest, and for reduction of sucker branch growth in hops. Permanent tolerances are established for the combined residues of endothall and its monomethyl ester at 0.1 ppm in/on cotton seeds, fish, dried hops and potatoes, and at 0.05 ppm in/on rice grain and straw [40 CFR §180.293(a)(1)].

In conjunction with a petition for tolerances on a wide variety of irrigated crops (PP# 8E7419), IR-4 has submitted field trial data reflecting irrigation of representative root and tuber vegetables with endothall-treated water. The chemical structure and nomenclature of endothall and its salts are listed in Table A.1. The physicochemical properties of technical grade endothall and its salts are listed in Table A.2.

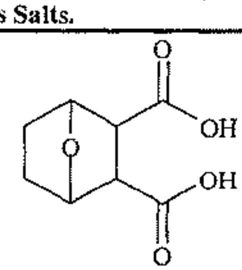
Table A.1. Structure and Nomenclature of Endothall and its Salts.	
Chemical Structure	
Common name	Endothall
Molecular Formula	$C_8H_{10}O_5$
Molecular Weight	186.16
IUPAC name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid
CAS name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid
CAS #	145-73-3
PC Code	038901
Current Food/Feed Site Registration	Cotton, hops, potato, alfalfa grown for seed

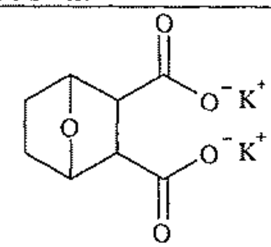
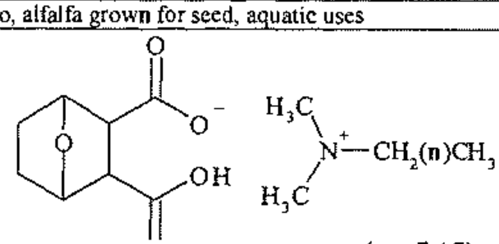
Table A.1. Structure and Nomenclature of Endothall and its Salts.	
Chemical Structure	
Common name	Endothall, dipotassium salt
Molecular Formula	$C_8H_8K_2O_5$
Molecular Weight	262.33
IUPAC name	Not available
CAS name	Not available
CAS #	2164-07-0
PC Code	038904
Current Food/Feed Site Registration	Cotton, hops, potato, alfalfa grown for seed, aquatic uses
Chemical Structure	 (n = 7-17)
Common name	Endothall, mono-N,N-dimethylalkyl amine salt
Molecular Formula	Not available
Molecular Weight	Average: 422
IUPAC name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid, compound with N,N-dimethylcocoamine
CAS name	Not available
CAS #	66330-88-9
PC Code	038905
Current Food/Feed Site Registration	Cotton, hops, potato, alfalfa grown for seed, aquatic uses

Table A.2. Physicochemical Properties of Endothall and Salts.		
Parameter	Value	Reference
Endothall (acid)		
Melting point	108-110℃	D187593, D187590, and D187588, 5/5/93, K. Dockter
pH	2.7 at 25℃ (1% solution)	D187593, D187590, and D187588, 5/5/93, K. Dockter
Density, bulk density, or specific gravity	0.481 g/cm^3 (bulk) at 25℃	D187593, D187590, and D187588, 5/5/93, K. Dockter
Water solubility at 25℃	109.8 g/L 13.1 g/100 mL in water, pH 5 12.7 g/100 mL in water, pH 7 12.5 g/100 mL in water, pH 9	D166798, 7/2/92, K. Dockter D207011, 9/30/94, F. Toghrol
Solvent solubility at 25℃	3.4 g/100 mL in acetonitrile 2.4 g/100 mL in n-octanol 16.0 g/100 mL in tetrahydrofuran	D207011, 9/30/94, F. Toghrol
Vapor pressure	3.92 x 10^{-5} mm Hg at 24.3℃	D166798, 7/2/92, K. Dockter

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Table A.2. Physicochemical Properties of Endothall and Salts.		
Parameter	Value	Reference
Dissociation constant, pK_a	4.32 for Step 1 and 6.22 for Step 2 at 20℃ (0.2% solution in 20% basic ethanol); dissociation rate 1.8-2.3 x 10^3 µmho within 3-5 minutes at □25℃, by conductivity meter	D188708, 5/3/93, K. Dockter
Octanol/water partition coefficient	Not applicable to endothall acid	D166798, 7/2/92, K. Dockter
UV/visible absorption spectrum	Not available	
Endothall, dipotassium salt		
Melting point	>360℃	D187593, D187590, and D187588, 5/5/93, K. Dockter
pH	9.1 at 25℃ (1% solution)	D187593, D187590, and D187588, 5/5/93, K. Dockter
Density, bulk density, or specific gravity	0.766 g/cm^1 (bulk) at 25℃	D187593, D187590, and D187588, 5/5/93, K. Dockter
Water solubility	>65 g/100 mL in water, pH 5, pH 7, and pH 9	D214691, 6/7/95, D. Hrdy
Solvent solubility	<0.001 g/100 mL in acetonitrile, n-octanol, and tetrahydrofuran	D214691, 6/7/95, D. Hrdy
Vapor pressure	Not applicable. An organic acid K salt is anticipated to have an insignificant vapor pressure.	D178085, 6/18/92, S. Funk
Dissociation constant, pK_a	4.16 for Step 1 and 6.14 for Step 2 at 20℃ in water; dissociation complete at 5 mins (13.6 x 10^3 µmho)	D304027, 6/10/2004, D. Soderberg
Octanol/water partition coefficient	K_{OW} <0.02 and <0.3 at concentrations of 9 x 10^{-3} M and 9 x 10^{-4} M, respectively, at 25℃	D210814, 8/9/95, S. Knizner
UV/visible absorption spectrum	Not available	
Endothall, mono-N,N-dimethylalkyl amine salt		
Boiling point	Not available	
pH	5.2 at 25℃ (1% solution)	D187593, D187590, and D187588, 5/5/93, K. Dockter
Density, bulk density, or specific gravity	1.028 g/mL at 25℃	D187593, D187590, and D187588, 5/5/93, K. Dockter
Water solubility at 25℃	≥49.2 g/100mL in water, pH 5 ≥51.6 g/100 mL in water, pH 7 ≥49.8 g/100 mL in water, pH 9	D210814, 8/9/95, S. Knizner
Solvent solubility at 25℃	≥102.5 g/100mL in acetonitrile ≥95.4 g/100 mL in n-octanol ≥104.3 g/100 mL in tetrahydrofuran	D210814, 8/9/95, S. Knizner
Vopor pressure	2.09 x 10^{-5} mm Hg at 25℃ (calculated; mixed mono- and dialkylamine (C8-C20))	D206344, 9/22/94, F. Toghrol
Dissociation constant, pK_a	4.24 for Step 1 and 6.07 for Step 2 at 20℃ for mixed mono- and dialkylamine (C8-C20) in acidified ethanol/water; dissociation complete □17 minutes (1.7 x 10^3 µmho) at 25℃	D198885, 4/7/94, F. Toghrol
Octanol/water partition coefficient	K_{OW} 2.097 at concentrations of 8.9 x 10^{-3} M and 8.9 x 10^{-4} M, at 25℃	D209995, 1/20/95, L. Edwards
UV/visible absorption spectrum	Not available	

B. EXPERIMENTAL DESIGN

B.1. Study Site Information

During 2006-2007, two sugar beet field trials were conducted in Zones 5 and 10, two carrot field trials were conducted in Zones 5 and 10, and two potato field trials were conducted in Zones 5 and 11 (Table B.1.1). The irrigation water used in each test was treated with endothall (2.0 lb ae/gal SC/L monoalkylamine salt) at a concentration of ~5 ppm, acid equivalent. In addition, in the two sugar beet field trials, side-by-side test were also conducted using the dipotassium salt of endothall applied to the irrigation water at a concentration of 3.5 ppm, acid equivalent. HED notes that although the dipotassium salt was applied at a concentration of 5 ppm ai, this rate is equivalent to a concentration of 3.5 ppm, acid equivalent. The treated water was applied in each test during vegetative development as six broadcast foliar applications using overhead sprinklers, at RTIs of 6-8 days. A volume equivalent to ~1 acre inch of water (~27,000 gal/A) was applied for each application. Based on the concentration of the endothall and the amount of water applied, the application rates for the monoalkylamine salt of endothall were equivalent to 1.13-1.14 lb ae/A/application, for a total of 6.77-6.83 lb ae/A/season (Table B.1.3). The application rates for the dipotassium salt were equivalent to 0.80-0.81 lb ae/A/application, for a total of 4.80-4.88 lb ae/A/season. These rates are expected to be conservative relative to actual inadvertent applications.

TABLE B.1.1. Trial Site Conditions.

Trial Identification (City, State; Year)	Soil characteristics[1]			
	Type	%OM	pH	CEC (meq/100g)
Sugar Beet				
Conklin, MI 2007 MI$19	Loam	2.7	6.9	9.8
Arroyo Grande, CA 2007 CA$22	Sandy Loam	1.2	6.6	8.6
Carrot				
Ravenna, MI 2007 MI$20	Loamy Sand	2.1	6.2	7.3
Arroyo Grande, CA 2006 CA$06	Sandy Loam	1.9	5.7	12.6
Potato				
Conklin, MI 2007 MI$21	Loam	2.1	6.5	9.0
Payette, ID 2007 ID$23	Loam	2.6	6.4	21.2

[1] These parameters are optional except in cases where their value affects the use pattern for the chemical.

TABLE B.1.2. Water Characterization.

Study site	Water characteristics				
	Type	Hardness/Salinity	pH	Turbidity	Dissolved OM
Conklin, MI 2007 MI$19	Well	NR	NR	NR	NR
Arroyo Grande, CA 2007 CA$22	Well	NR	NR	NR	NR
Ravenna, MI 2007 MI$20	Well	NR	NR	NR	NR
Arroyo Grande, CA 2006 CA$06	Well	NR	NR	NR	NR
Conklin, MI 2007 MI$21	Well	NR	NR	NR	NR
Payette, ID 2007 ID$23	Well	NR	NR	NR	NR

NR = not reported.

The actual temperature recordings and rainfall were typical for each site and no unusual weather conditions were reported. Aside from the treated-irrigations, no other irrigation was reported during the study period. The tests were conducted according to normal agricultural practices for the regions, and information was provided on maintenance pesticides and fertilizers used at each site. No information was provided on the characteristics of the water used for irrigation, other than the source (Table B.1.2).

TABLE B.1.3. Study Use Pattern.

Location (City, State; Year) Trial ID	End-Use Product [1]	Application Information					
		Method; Timing	Concen. (ppm) [2]	Volume (gal/A) [3]	Single Rate (lb ae/A) [4]	RTI (days) [5]	Total Rate (lb ae/A) [1]
Sugar Beet							
Conklin, MI 2007 MI$19	2.0 lb/gal SC/L	Six overhead sprinkler applications during vegetative development	4.98	27,156-27,160	1.13	7	6.77
	3.0 lb/gal SC	Six overhead sprinkler applications during vegetative development	3.5		0.80	7	4.80
Arroyo Grande, CA 2007 CA$22	2.0 lb/gal SC/L	Six overhead sprinkler applications during vegetative development	4.98	27,149	1.13	7-8	6.79
	3.0 lb/gal SC/L	Six overhead sprinkler applications during vegetative development	3.5		0.81	7-8	4.88
Carrot							
Ravenna, MI 2007 MI$20	2.0 lb/gal SC/L	Six overhead sprinkler applications during vegetative development	4.98	27,149-27,161	1.13	6-7	6.77
Arroyo Grande, CA 2006 CA$06	2.0 lb/gal SC/L	Six overhead sprinkler applications during vegetative development	4.98	27,148	1.13	6-8	6.79
Potato							
Conklin, MI 2007 MI$21	2.0 lb/gal SC/L	Six overhead sprinkler applications during vegetative development	4.98	27,154-27,160	1.13	7	6.77
Payette, ID 2007 ID$23	2.0 lb/gal SC/L	Six overhead sprinkler applications during vegetative development	5.04	27,117	1.14	7-8	6.83

1 The two formulations used are expressed in lb acid equivalent/gal. The monoalkylamine salt is a 2.0 lb ae/gal SC/L and the dipotassium salt is a 3.0 lb ae/gal SC/L. When applied according to the label directions, the maximum concentration for endothall (free acid) is 5 ppm for the monoalkylamine salt and 3.5 ppm for the dipotassium salt.
2 The concentration of endothall (in acid equivalents) in the irrigation water. No adjuvants were included in the irrigation water.
3 The target irrigation rate was 1 acre inch of water or 27,154 gal/A.
4 The equivalent field use rates were calculated by the reviewer based on the concentration of the endothall (ae), the application volume and plot size.
4 RTI = Retreatment Interval.

TABLE B.1.4. Trial Numbers and Geographical Locations.

NAFTA Growing Zones	Carrot			Potato			Sugar beet		
	Submitted	Requested [1]		Submitted	Requested [1]		Submitted	Requested [1]	
		Canada	U.S.		Canada	U.S.		Canada	U.S.
1	--	--	--	--	3	2	--	--	--
1A	--	1	--	--	4	--	--	--	--
2	--	--	--	--	--	--	--	--	--
3	--	--	1	--	--	1	--	--	--
4	--	--	--	--	--	1	--	--	--
5	1	2	1	1	3	--	1 [2]	2	5
5A	--	--	--	--	1	--	--	--	--
5B	--	2	--	--	1	--	--	--	--
6	--	--	1	--	--	4	--	--	1
7	--	--	--	--	--	--	--	--	--
7A	--	--	--	--	--	1	--	2	1
8	--	--	--	--	--	--	--	--	1
9	--	--	--	--	--	--	--	--	2
10	1	--	4	--	--	1	1 [2]	--	2
11	--	--	1	1	--	1	--	--	--
12	--	--	--	--	1	6	--	--	--
13	--	--	--	--	--	--	--	--	--
Total	2	5	8 [6] [3]	2	16	16 [12] [3]	2	5	12 [9] [3]

1 Based on EPA OPPTS Guideline 860.1500.
2 The two sugar beet field trial included side-by-side tests compared the monoalkylamine and dipotassium salts of endothall (total of 4 tests).
3 The number in brackets indicates the 25% reduction in the number of field trials allowed for support a crop group tolerance.

B.2. Sample Handling and Preparation

Sugar beet tops and roots, carrot roots, and potato tubers were harvested at 0 DAT (after the sixth application). A single control and duplicate treated samples of sugar beet roots and tops (≥5.25 lbs/sample), carrot roots (≥5.75 lbs/sample), and potato tubers (≥10.5 lbs/sample) were collected from each test and placed in frozen storage at each test facility within 3 hours. Samples were stored frozen at the field sites for 1-27 days. Samples were then shipped by ACDS freezer truck to the analytical laboratory, United Phosphorus, Inc. (King of Prussia, PA), and stored frozen (≤-18EC) until analysis.

B.3. Analytical Methodology

Residues of endothall (free acid) in/on carrots, potatoes and sugar beets (tops and roots) were determined using a LC/MS/MS method (Method No. KP-242R1) entitled "Analytical Method for Determination of Endothall in Crops", issued 5/4/2007.

For this method, residues were extracted twice by homogenization with water followed by centrifugation and filtering. Residues were then derivatized with HFTH in 50% H_3PO_4 at 100-120°C for 90 minutes. After cooling, the derivatized residues were partitioned into MTBE, evaporated to dryness, and reconstituted in hexane:MTBE (1:1 v:v). Residues were then cleaned using an amine SPE cartridge eluted with methanol:MTBE (1:4). Residues were analyzed by LC/MS/MS using external standards. The m/z 397→166 ion transition was used for quantifying residues, and residues are expressed in endothall acid equivalents. The validated LOQ for endothall in/on onions is 0.05 ppm. An LOD of 0.00001 ppm was reported; however, this value was the instrument LOD, rather than the LOD of residue in a control matrix.

The above method was validated prior to and in conjunction with the analysis of the field trial samples. Control samples of carrot and sugar beet roots were fortified with endothall at 0.05-5.0 ppm for method validation. For concurrent recoveries, control samples were fortified with endothall at 0.05-0.1 ppm for carrot root, 0.05-0.5 ppm for potato tuber and sugar beet root, and 0.05-2.0 ppm for sugar beet tops.

C. RESULTS AND DISCUSSION

The LC/MS/MS method used for determining residues of endothall in/on sugar beet, carrot, and potato was adequately validated prior to and in conjunction with the analysis of field trial samples. The average method validation recoveries (±S.D.) were 76 ± 5% for carrot root and 82 ± 8% for sugar beet root. The average concurrent recoveries (±S.D) were 78 ± 3% for carrot root, 80 ± 8% for potato tuber, 81 ± 5% for sugar beet tops and 79 ± 8% for sugar beet root. Apparent residues of endothall were <LOQ in/on control samples of each matrix. Adequate sample calculations and example chromatograms were provided, and the fortification levels used for the method recoveries were similar in magnitude to the measured residue levels.

Carrot, potato, and sugar beet samples were stored at <-18°C for up to 272, 58, and 64 days, respectively, prior to analysis (Table C.2). Adequate storage stability data are available indicating that endothall is stable in frozen lettuce and sugar beet roots for up to 465 days (47520719.der, under review). The stability data for lettuce and beet roots will support the storage durations and conditions for the current field trials.

Following six overhead sprinkler applications with irrigation water containing the monoalkylamine salt of endothall at 5 ppm, acid equivalents (6.77-6.83 lb ae/A/season), endothall residues at 0 DAT were 1.11-1.62 ppm in/on 4 samples of sugar beet tops, 0.136-0.591 ppm in/on 4 samples of sugar beet roots, 0.062-0.088 ppm in/on 4 samples of carrot roots, and 0.067-0.103 ppm in/on 4 samples of potato tubers (Table C.3). Average endothall residues were 1.34 ppm for sugar beet tops, 0.330 ppm for sugar beet roots, 0.078 ppm for carrot roots, and 0.080 ppm for potato tubers (Table C.4). The HAFT residues were 1.37 ppm for sugar beet tops, 0.493 ppm for sugar beet roots and 0.088 ppm for both carrot roots and potato tubers. No residue decline data was provided.

Following six overhead sprinkler applications with irrigation water containing the dipotassium salt of endothall at 3.5 ppm, acid equivalents (4.80-4.88 lb ae/A/season), endothall residues at 0 DAT were 0.523-1.28 ppm in/on 4 samples of sugar beet tops and 0.115-0.345 ppm in/on 4 samples of sugar beet roots. Average endothall residues were 0.821 ppm in/on sugar beet tops and 0.224 ppm in/on sugar beet roots, and HAFT residues in/on sugar beet tops and roots were 1.11 and 0.331 ppm, respectively.

Although average endothall residues in/on sugar beet tops and roots were clearly lower (0.6-0.7x) for the dipotassium salt formulation than for the monoalkylamine salt formulation, direct comparison of the two formulations is not possible because the two formulations were applied at different rates. The monoalkylamine salt was applied at 5 ppm acid equivalents; however, the dipotassium salt was applied at only 3.5 ppm acid equivalent, 0.7x the rate of the monoalkylamine salt. As explained previously, these different application rates are consistent with the two different labels.

Common cultural practices were used to maintain plants, and the weather conditions and maintenance chemicals and fertilizer used in this study are not expected to have had a notable impact on the residue data. No phytotoxicity was reported in any of the tests.

TABLE C.1. Summary of Method Validation and Concurrent Recoveries of Endothall from Carrot, Potato and Sugar beet.

Matrix	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean ± Std. Dev. [1] (%)
Method Validation				
Carrot, root	0.05	3	78, 71, 72	74 ± 4
	0.5	3	74, 73, 73	73 ± 1
	5.0	3	86, 80, 78	81 ± 4
	Total	**9**	**71-86**	**76 ± 5**
Sugar beet, root	0.05	3	71, 73, 74	73 ± 2
	0.5	3	89, 81, 78	83 ± 6
	5.0	3	95, 90, 83	89 ± 6
	Total	**9**	**71-95**	**82 ± 8**
Concurrent Recoveries				
Carrot, root	0.05	2	75, 79	77
	0.1	2	75, 82	79
	Total	**4**	**75-82**	**78 ± 3**
Potato, tuber	0.05	2	83, 89	86
	0.25	1	78	78
	0.5	1	71	81
	Total	**4**	**71-89**	**80 ± 8**
Sugar beet, tops	0.05	2	84, 75	80
	1.0	1	86	86
	2.0	1	78	78
	Total	**4**	**75-86**	**81 ± 5**
Sugar beet, root	0.05	2	74, 73	74
	0.5	2	90, 79	85
	Total	**4**	**73-90**	**79 ± 8**

[1] Standard deviations were calculated only for datasets having ≥3 values.

TABLE C.2. Summary of Storage Conditions.

Matrix	Storage Temperature (°C)	Actual Storage Duration (days)[1]	Interval of Demonstrated Storage Stability (days)[2]
Carrot	≤-18	33-272	465
Potato		41-58	
Sugar beet tops		47-64	
Sugar beet roots		47-64	

1 Interval from harvest to extraction for analysis. Extracts were stored 0-5 days prior to analysis.
2 Endothall is stable in frozen lettuce and sugar beet roots for up to 467 days (47520719.der under review).

TABLE C.3. Residue Data from Root and Tuber Vegetable Field Trials with Endothall.

Trial ID (City, State; Year)	Zone	Crop; Variety	Matrix	Total Rate ppm	Total Rate lb ae/A	PHI (days)	Residues (ppm)[1,2]	
Sugar Beets								
Conklin, MI 2007 MI$19	5	Sugar beet; Beta 5451	Tops	5.0	6.77	0	1.256	1.374
				3.5	4.80	0	0.523	0.531
			Roots	5.0	6.77	0	0.199	0.136
				3.5	4.80	0	0.120	0.115
Arroyo Grande, CA 2007 CA$22	10	Sugar beet; Alpine Medium Quickprime	Tops	5.0	6.79	0	1.618	1.105
				3.5	4.88	0	1.279	0.948
			Roots	5.0	6.79	0	0.591	0.395
				3.5	4.88	0	0.345	0.316
Carrot								
Ravenna, MI 2007 MI$20	5	Carrot; Recoleta	Root	5.0	6.77	0	0.075	0.062
Arroyo Grande, CA 2006 CA$06	10	Carrot; Nantes	Root	5.0	6.79	0	0.088	0.088
Potato								
Conklin, MI 2007 MI$21	5	Potato; Dark Red Norland	Tuber	5.0	6.77	0	0.072	0.103
Payette, ID 2007 ID$23	11	Potato; Ranger Russet	Tuber	5.0	6.83	0	0.067	0.078

1 Expressed in endothall acid equivalent. The LOQ is 0.05 ppm.
2 The two values in each row represent two samples from a single plot.

TABLE C.4. Summary of Residue Data from Root and Tuber Vegetable Field Trials with Endothall.

Commodity	Formulation type	Total Applic. Rate [1]	PHI (days)	Residue Levels (ppm) [2]						
				n	Min.	Max.	HAFT [3]	Median (STMdR)	Mean (STMR)	Std. Dev.
Sugar beet, tops	Monoamine salt (SC/L)	5 ppm (6.77-6.79)	0	2	1.32	1.36	1.36	1.34	1.34	0.033
	Dipotassium salt (SC/L)	3.5 ppm (4.80-4.88)	0	2	0.527	1.114	1.114	0.820	0.820	0.415
Sugar beet, roots	Monoamine salt (SC/L)	5 ppm (6.77-6.79)	0	2	0.165	0.493	0.493	0.330	0.330	0.230
	Dipotassium salt (SC/L)	3.5 ppm (4.80-4.88)	0	2	0.118	0.330	0.331	0.224	0.224	0.151
Carrot	Monoamine salt (SC/L)	5 ppm (6.77-6.79)	0	2	0.0685	0.088	0.088	0.078	0.078	0.014
Potato	Monoamine salt (SC/L)	5 ppm (6.77-6.83)	0	2	0.0725	0.875	0.0875	0.080	0.080	0.011

1 The concentration are expressed in acid equivalents, and the values in parentheses are the total application rate in terms of lb ae/A.
2 Residues are expressed in terms of the free acid. The LOQ is 0.05 ppm.
3 HAFT = Highest Average Field Trial.

D. CONCLUSION

The available field trial data are adequate and support the use of endothall-treated water for irrigation of root and tuber vegetables. The data support the use of endothall (monoalkylamine salt) in irrigation water at a concentration of 5 ppm (ae), with no more than six applications to the water per season and a minimum 7-day interval of application of treated water to vegetable crops. Results represent a 0-day PHI. However, the data are not appropriate for directly comparing residues resulting from the use of the dipotassium salt formulation with the monoalkylamine salt formulation because the dipotassium salt was applied at a lower rate (0.7x).

E. REFERENCES

None

F. DOCUMENT TRACKING

RDI: D. Soderberg (5 June 2009), W. Donovan (5 June 2009)
Petition Number: 8E7419
DP#: 356315
PC Code: 038901, 038904, and 038905

Template Version June 2005

Primary Evaluator [signature] Date: 5 June 2009
David Soderberg, Chemist, RABV, HED

Approved by [signature] Date: 5 June 2009
William Donovan, Senior Scientist, RABV, HED

This DER was originally prepared under contract by Dynamac Corporation (1910 Sedwick Road, Building 100, Suite B, Durham, NC 27713; submitted 3/25/2009). The DER has been reviewed by the Health Effects Division (HED) and revised as needed for clarity, correctness and to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORT:

47520701. Arsenovic, M. (2008) Endothall (Hydrothol 191 and Aquathol K): Magnitude of the Residue on Vegetable, Root and Tuber Group: Lab Project Number: Z9762. Unpublished study prepared by Interregional Research Project No. 4. 389 pages.

EXECUTIVE SUMMARY:

Interregional Research Project No. 4 (IR-4) submitted a sugar beet processing study reflecting the exposure of sugar beets to endothall through the use of treated irrigation water. In a field trial conducted in CA (Zones 10) during 2007, a 2.0 lb ae/gal soluble concentrate (SC/L) formulation of endothall (monoalkylamine salt) was used to treat the irrigation water at a rate of 5 ppm ae. [In order to avoid the complications of different molecular weights for different salts, endothall concentrations are expressed as the free acid equivalents (ae).] The treated water was then applied using overhead sprinklers to the sugar beets as six broadcast foliar applications during vegetative development at retreatment intervals (RTIs) of 7-8 days. A volume equivalent to 1 acre inch of water (~27,154 gal/A) was applied for each application. Based on the concentration of the endothall and the amount of water applied, the application rate for endothall was equivalent to 1.13 lb ae/A/application, for a total of 6.79 lb ae/A/season.

Single bulk control and treated samples of sugar beet roots were harvested at normal crop maturity, immediately following the last irrigation (0 days after treatment, DAT). The roots were washed and processed into dried pulp, molasses, and refined sugar using simulated commercial procedures. Samples of unwashed whole roots were stored frozen for up to 64 days prior to analysis, and samples of each processed fractions were stored frozen for up to 24 days prior to analysis. The sample storage intervals and conditions are supported by the available storage stability data.

Residues of endothall (free acid) in/on sugar beet roots and processed fractions were determined using an adequate LC/MS/MS method (Method No. KP-242R1). Residues in roots and dried pulp samples were extracted with water and then derivatized with heptafluoro-*p*-tolylhydrazine (HFTH) in 50% H_3PO_4. Sugar and molasses samples were initially dissolved in water and then residues were derivatized. The derivatized residues from each matrix were cleaned up by partitioning into methyl t-butyl ether (MTBE) and elution through an amine solid phase extraction (SPE) cartridge. Residues were then analyzed by LC/MS/MS using external standards for quantitation. The validated limit of quantitation (LOQ) for endothall is 0.05 ppm in each sugar beet matrix.

Residues of endothall averaged 0.493 ppm in/on whole unwashed roots (RAC) and were 0.554 ppm in dried pulp, 1.203 in molasses, and <0.05 ppm in refined sugar. The processing factors were 1.1x for dried pulp, 2.4x for molasses, and <0.1x for refined sugar. The theoretical concentration factor for refined sugar is 12.5x.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the sugar beet processing study is classified as scientifically acceptable. The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document, DP# 356315.

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported which would have an adverse impact on the validity of the study.

A. BACKGROUND INFORMATION

Endothall [7-oxabicyclo[2,2,1] heptane-2,3-dicarboxylic acid] is a selective contact herbicide, defoliant, desiccant, and aquatic algicide that belongs to the dicarboxylic acid chemical class. The free acid of endothall (PC Code 038901) and its dipotassium (PC Code 038904) and alkylamine (PC Code 038905) salts are registered primarily as aquatic herbicides for the control a variety of plants in water bodies. This includes irrigation canals, but with a 7 day holding time. They are also registered for desiccation/defoliation of alfalfa/clover (grown for seed only), cotton, and potatoes prior to harvest, and for reduction of sucker branch growth in hops. Permanent tolerances are established for the combined residues of endothall and its monomethyl ester at 0.1 ppm in/on cotton seeds, fish, dried hops and potatoes, and at 0.05 ppm in/on rice grain and straw [40 CFR §180.293(a)(1)].

In conjunction with a petition for tolerances on a wide variety of irrigated crops (PP# 8E7419), IR-4 has submitted a sugar beet processing study reflecting irrigation of sugar beets with endothall-treated water. The chemical structure and nomenclature of endothall and its amine salt are listed in Table A.1. The physicochemical properties of technical grade endothall and its amine salt are listed in Table A.2.

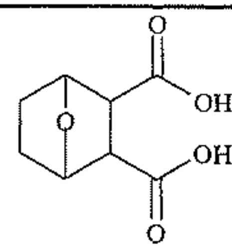
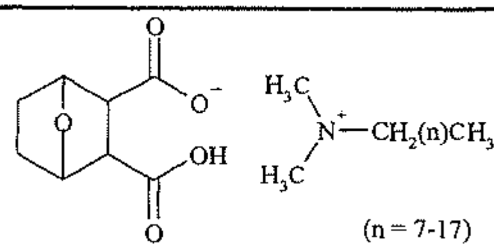
Table A.1. Endothall and Salts Nomenclature	
Chemical Structure	
Common name	Endothall
Molecular Formula	$C_8H_{10}O_5$
Molecular Weight	186.16
IUPAC name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid
CAS name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid
CAS #	145-73-3
PC Code	038901
Current Food/Feed Site Registration	Cotton, hops, potato, alfalfa grown for seed
Chemical Structure	 (n = 7-17)
Common name	Endothall, mono-N,N-dimethylalkyl amine salt
Molecular Formula	Not available
Molecular Weight	Average: 422
IUPAC name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid, compound with N,N-dimethylcocoamine
CAS name	Not available
CAS #	66330-88-9
PC Code	038905
Current Food/Feed Site Registration	Cotton, hops, potato, alfalfa grown for seed, aquatic uses

Table A.2. Physicochemical Properties of Endothall and Salts		
Parameter	Value	Reference
Endothall (acid)		
Melting point	108-110°C	D187593, D187590, and D187588, 5/5/93, K. Dockter
pH	2.7 at 25°C (1% solution)	D187593, D187590, and D187588, 5/5/93, K. Dockter
Density, bulk density, or specific gravity	0.481 g/cm^3 (bulk) at 25°C	D187593, D187590, and D187588, 5/5/93, K. Dockter
Water solubility at 25°C	109.8 g/L 13.1 g/100 mL in water, pH 5 12.7 g/100 mL in water, pH 7 12.5 g/100 mL in water, pH 9	D166798, 7/2/92, K. Dockter D207011, 9/30/94, F. Toghrol
Solvent solubility at 25°C	3.4 g/100 mL in acetonitrile 2.4 g/100 mL in n-octanol 16.0 g/100 mL in tetrahydrofuran	D207011, 9/30/94, F. Toghrol
Vapor pressure	3.92 x 10^{-5} mm Hg at 24.3°C	D166798, 7/2/92, K. Dockter
Dissociation constant, pK_a	4.32 for Step 1 and 6.22 for Step 2 at 20°C (0.2% solution in 20% basic ethanol); dissociation rate 1.8-2.3 x 10^3 µmho within 3-5 minutes at □25°C, by conductivity meter	D188708, 5/3/93, K. Dockter
Octanol/water partition coefficient	Not applicable to endothall acid	D166798, 7/2/92, K. Dockter
UV/visible absorption spectrum	Not available	
Endothall, mono-N,N-dimethylalkyl amine salt		
Boiling point	Not available	
pH	5.2 at 25°C (1% solution)	D187593, D187590, and D187588, 5/5/93, K. Dockter
Density, bulk density, or specific gravity	1.028 g/mL at 25°C	D187593, D187590, and D187588, 5/5/93, K. Dockter
Water solubility at 25°C	≥49.2 g/100mL in water, pH 5 ≥51.6 g/100 mL in water, pH 7 ≥49.8 g/100 mL in water, pH 9	D210814, 8/9/95, S. Knizner
Solvent solubility at 25°C	≥102.5 g/100mL in acetonitrile ≥95.4 g/100 mL in n-octanol ≥104.3 g/100 mL in tetrahydrofuran	D210814, 8/9/95, S. Knizner
Vapor pressure	2.09 x 10^{-5} mm Hg at 25°C (calculated; mixed mono- and dialkylamine (C8-C20))	D206344, 9/22/94, F. Toghrol
Dissociation constant, pK_a	4.24 for Step 1 and 6.07 for Step 2 at 20°C for mixed mono- and dialkylamine (C8-C20) in acidified ethanol/water; dissociation complete □17 minutes (1.7 x 10^3 µmho) at 25°C	D198885, 4/7/94, F. Toghrol
Octanol/water partition coefficient	K_{OW} 2.097 at concentrations of 8.9 x 10^{-3} M and 8.9 x 10^{-4} M, at 25°C	D209995, 1/20/95, L. Edwards
UV/visible absorption spectrum	Not available	

B. EXPERIMENTAL DESIGN

B.1. Application and Crop Information

In a field trial conducted in CA during 2007, sugar beets were irrigated six times with endothall-treated water using overhead sprinklers (Table B.1.1). The irrigation water was treated with endothall (2.0 lb ae/gal SC/L monalkylamine salt) at a concentration of ~5 ppm, acid equivalent. The beets were irrigated six times during vegetative development at RTIs of 7-8 days. A volume equivalent to ~1 acre inch of water (27,154 gal/A) was applied for each irrigation. Based on the

concentration of the endothall and the amount of water applied, application rate for endothall was equivalent to 1.13 lb ae/A/application, for a total of 6.79 lb ae/A/season.

TABLE B.1.1. Study Use Pattern.

Location (City, State; Year) Trial ID	End-Use Product	Application Information					
		Method; Timing	Concn. (ppm) [1]	Volume (gal/A) [2]	Single Rate (lb ac/A) [3]	RTI [4] (days)	Total Rate (lb ae/A) [3]
Arroyo Grande, CA 2007 CAS22	2.0 lb ae/gal SC/L	Six broadcast foliar applications during vegetative development using overhead sprinklers.	5.0	27,149	1.13	7-8	6.79

[1] The concentrate of endothall (in acid equivalents) in the irrigation water. No adjuvants were included in the irrigation water.
[2] The target irrigation rate was 1 acre inch of water or 27,154 gal/A.
[3] The equivalent field use rates were calculated by the reviewer based on the concentration of the endothall (ae), the application volume and plot size.
[4] RTI = Retreatment Interval.

B.2. Sample Handling and Processing Procedures

Single bulk control and treated samples (105 lbs/sample) of sugar beet roots were harvested at 0 DAT. The samples were frozen within 3 hours of harvest and shipped frozen on the day of harvest to the processing facility, GLP Technologies (Navasota, TX), where samples were stored at ≤-12°C until processing. Processing was initiated and completed within 36 days of harvest. Prior to processing, two subsamples of unwashed roots (RAC) were collected for analysis. The remaining samples were processed into molasses, sugar and dried pulp using simulated commercial procedures (Figure B.1). After processing, the root samples and each processed fraction were stored at ≤-12°C.

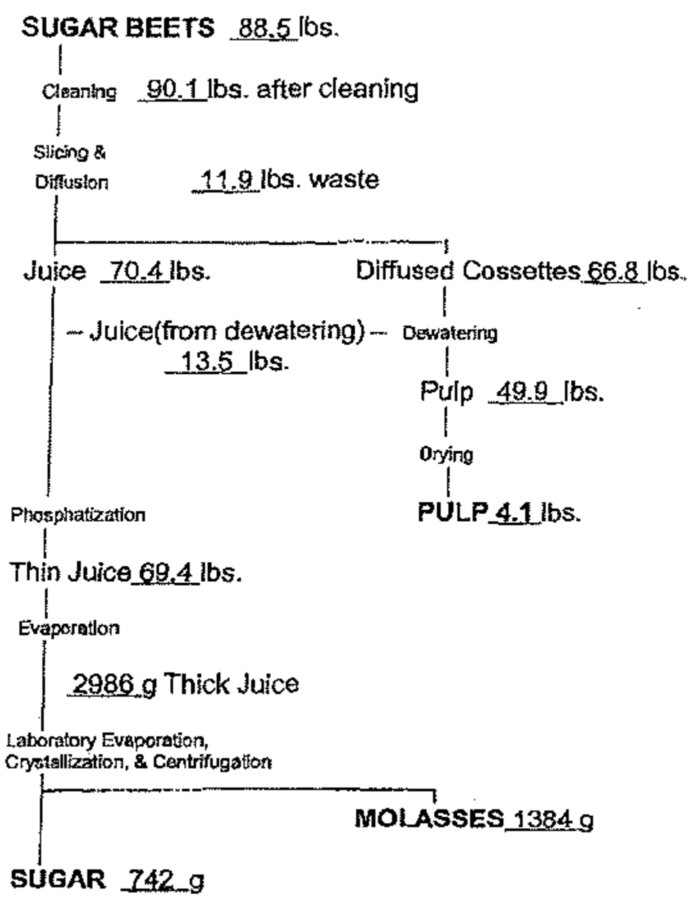
Within 3 days of processing, the frozen root and processed fraction samples were shipped by overnight courier on dry ice to the analytical laboratory, United Phosphorous, Inc. (King of Prussia, PA), where the samples were processed and stored at -18°C until analysis.

Figure B.1. Processing Flowchart for Treated Sugar Beet Roots.

FORM H.211 Revision 00

SUGAR BEET PROCESSING MATERIAL BALANCE

Sample # 2 (Treated, Trt. 02) Code # N



B.3. Analytical Methodology

Residues of the free acid of endothall in/on sugar beet roots and its processed fractions were determined using a LC/MS/MS method (Method No. KP-242R1) entitled "Analytical Method for Determination of Endothall in Crops", issued 5/4/2007.

For this method, residues in root and pulp were extracted twice by homogenization with water followed by centrifugation and filtering. For molasses and refined sugar, the samples were initially dissolved in water. Residues were then derivatized with HFTH in 50% H_3PO_4 at 100-

120°C for 90 minutes. After cooling, the derivatized residues were partitioned into MTBE, evaporated to dryness, and reconstituted in hexane:MTBE (1:1 v:v). Residues were then cleaned using an amine SPE cartridge eluted with methanol:MTBE (1:4). Residues were analyzed by LC/MS/MS using external standards. The m/z 397→166 ion transition was used for quantifying residues, and residues are expressed in acid equivalents. The validated LOQ for endothall is 0.05 ppm. An LOD of 0.00001 ppm was reported; however, this value was the instrument LOD, rather than the LOD of residue in a control matrix.

For method validation, control samples of sugar beet roots and molasses were fortified with endothall at 0.05-5.0 ppm. For concurrent recoveries, control sample were fortified with endothall at 0.05 and 0.5 ppm for roots and each processed fraction.

C. RESULTS AND DISCUSSION

The LC/MS/MS method used for determining residues of endothall in/on sugar beet roots and its processed fractions was adequately validated prior to and in conjunction with the analysis of processing study samples (Table C.1). Method validation recoveries averaged (±SD) 82 ± 8% from whole roots and 90 ± 12% from molasses. Concurrent recoveries averaged 79% for whole roots, 81% for refined sugar, 80% for dried pulp, and 76% for molasses. Apparent residues of endothall were <LOQ in/on control samples of each matrix. Adequate sample calculations and example chromatograms were provided and the fortification levels used for method recoveries were similar in magnitude to the measured residue levels.

Sugar beet roots were stored at -18°C for up to 64 days prior to analysis, and the processed fractions were stored at -18°C for up to 24 days prior to analysis (Table C.2). As the processed fractions were analyzed within one month of sampling, supporting storage stability data are not required for the processed fractions. Adequate storage stability data are available indicating that endothall is stable in frozen sugar beet roots for up to 465 days (47520719.der, under review). These stability data will support the storage durations and conditions for the processing study.

Residues of endothall averaged 0.493 ppm in/on whole unwashed roots (RAC) and were 0.123 ppm in/on washed roots, 0.554 ppm in dried pulp, 1.203 ppm in molasses, and <0.05 ppm in refined sugar (Table C.3). The calculated processing factors were 0.2x for washed roots, 1.1x for dried pulp, 2.4x for molasses, and <0.1x for refined sugar. The theoretical concentration factor is 12.5x for refined sugar.

TABLE C.1. Summary of Method Validation and Concurrent Recoveries of Endothall from Sugar Beet Roots and Its Processed Fractions.

Matrix	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean ± Std. Dev. [1] (%)
Method Validation				
Sugar beet, root	0.05	3	71, 73, 74	73 ± 2
	0.5	3	89, 81, 78	83 ± 6
	5.0	3	95, 90, 83	89 ± 6
	Total	**9**	**71-95**	**82 ± 8**
Sugar beet, molasses	0.05	3	80, 84, 97	87 ± 9
	0.5	3	84, 82, 100	89 ± 10
	5.0	3	74, 114, 91	93 ± 20
	Total	**9**	**74-114**	**90 ± 12**
Concurrent Recoveries				
Sugar beet root	0.05	2	74, 73	74
	0.5	2	90, 79	85
	Total	4	73-90	**79 ± 8**
Sugar beet, refined sugar	0.05	1	74	81
	0.5	1	89	
Sugar beet, dried pulp	0.05	1	75	80
	0.5	1	85	
Sugar beet, molasses	0.05	1	79	76
	0.5	1	73	

[1] Standard deviations are calculated for data sets having ≥3 values.

TABLE C.2. Summary of Storage Conditions for Sugar Beet Matrices.

Matrix	Storage Temperature (°C)	Actual Storage Duration (days)[1]	Interval of Demonstrated Storage Stability (days)[2]
Roots	-18	30-64	467
Refined sugar		19-21	
Dried pulp		22-24	
Molasses		21-23	

[1] Interval from harvest to extraction for analysis. Extracts were stored 0-5 days prior to analysis.
[2] Endothall is stable in frozen sugar beet roots for up to 465 days (47520719.der under review).

TABLE C.3. Residue Data from Sugar Beet Processing Study with Endothall.

RAC	Processed Commodity	Total Rate [1]	PHI (days)	Residues (ppm) [2]	Processing Factor
Sugar beet	Unwashed roots (RAC)	5 ppm (6.79 lb ae/A)	0	0.591, 0.395 (ave. 0.493)	--
	Washed roots			0.123	0.2x
	Dried pulp			0.554	1.1x
	Molasses			1.203	2.4x
	Refined sugar			<0.05	<0.1x

[1] The rate is expressed both in terms of the concentration in the irrigation water (ppm) and the total amount (lb ae/A) applied.
[2] Residues are expressed in acid equivalents. The LOQ is 0.05 ppm.

D. CONCLUSION

The sugar beet processing study is adequate. Endothall residues did not concentrate in refined sugar (<0.1x), but concentrated slightly (1.1x) in dried pulp and by 2.4x in molasses.

E. REFERENCES

None

F. DOCUMENT TRACKING

RDI: David Soderberg (5 June 2009); William Donovan (5 June 2009)
Petition Number: 8E7419
DP#: 356315
PC Code: 038901, 038905

Template Version June 2005

Primary Evaluator	David Soderberg David Soderberg, Chemist, RABV/HED	Date: 5 June 2009
Approved by	William H. Donovan William Donovan, Senior Scientist, RABV, HED	Date: 5 June 2009

This DER was originally prepared under contract by Dynamac Corporation (1910 Sedwick Road, Building 100, Suite B, Durham, NC 27713; submitted 3/25/2009). The DER has been reviewed by the Health Effects Division (HED) and revised as needed for clarity, correctness and to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORT:

47520702. Arsenovic, M. (2008) Endothall (Hydrothol 191): Magnitude of the Residue on Vegetable Bulb Group: Lab Project Number: Z9763. Unpublished study prepared by Interregional Research Project No. 4. 185 pages.

EXECUTIVE SUMMARY:

Interregional Research Project No. 4 (IR-4) submitted field trial data reflecting the exposure of green and dry bulb onions to endothall through the use of treated irrigation water. In a green onion and dry bulb onion field trial conducted during 2007 in Zones 6 and 10, respectively, a 2.0 lb ae/gal soluble concentrate (SC/L) formulation of endothall (monoalkylamine salt) was used to treat the irrigation water at a rate of 5 ppm ae. [In order to avoid the complications of different molecular weights for the different salts, endothall concentrations are expressed as the free acid equivalents (ae).] The treated water was applied to onions during vegetative development as six broadcast foliar applications using overhead sprinklers, at retreatment intervals (RTIs) of 7-8 days. A volume equivalent to ~1 acre inch of water (27,154 gal/A) was applied for each application. Based on the concentration of the endothall and the amount of water applied, the application rates for endothall were equivalent to 1.12-1.13 lb ae/A/application, for a total of 6.75-6.76 lb ae/A/season.

Single control and duplicate treated samples of green onions and dry bulb onions were harvested from the respective tests on the day of the final application (0 days after treatment, DAT), and samples were stored at <-18°C for up to 143 days prior to analysis. Adequate storage stability data are available to support the duration and conditions of sample storage.

Residues of endothall (free acid) in/on onions were determined using an adequate LC/MS/MS method (Method No. KP-242R1). For this method, residues were extracted with water and then derivatized with heptafluoro-*p*-tolylhydrazine (HFTH) in 50% H_3PO_4. The derivatized residues were cleaned up by partitioning into methyl t-butyl ether (MTBE) and elution through an amine solid phase extraction (SPE) cartridge. Residues were then analyzed by LC/MS/MS using external standards for quantitation. Residues are expressed in endothall acid equivalents. The validated limit of quantitation (LOQ) for endothall in/on onions is 0.05 ppm.

Following six overhead sprinkler applications with irrigation water containing endothall at 5 ppm (6.75-6.76 lb ae/A/season), endothall residues at 0 DAT were 0.234 and 0.0284 ppm in/on 2 samples of green onions and <0.05 ppm in/on 2 samples of dry bulb onions. The average residues were 0.259 ppm for green onions and <0.05 ppm for dry bulb onions. No residue decline data was provided.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the field trial residue data are scientifically acceptable. Although only one trial was performed for each crop, the results are expected to be conservative. The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document, DP# 356315.

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported which would have an adverse impact on the validity of the study.

A. BACKGROUND INFORMATION

Endothall [7-oxabicyclo[2,2,1] heptane-2,3-dicarboxylic acid] is a selective contact herbicide, defoliant, desiccant, and aquatic algicide that belongs to the dicarboxylic acid chemical class. The free acid of endothall (PC Code 038901) and its dipotassium (PC Code 038904) and alkylamine (PC Code 038905) salts are registered primarily as aquatic herbicides for the control a variety of plants in water bodies. This includes irrigation canals, but only with a 7 day holding period. They are also registered for desiccation/ defoliation of alfalfa/clover (grown for seed only), cotton, and potatoes prior to harvest, and for reduction of sucker branch growth in hops. Permanent tolerances are established for the combined residues of endothall and its monomethyl ester at 0. 1 ppm in/on cotton seeds, fish, dried hops and potatoes, and at 0.05 ppm in/on rice grain and straw [40 CFR §180.293(a)(1)].

In conjunction with a petition for tolerances on a wide variety of irrigated crops (PP# 8E7419), IR-4 has submitted field trial data reflecting irrigation of green and dry bulb onions with endothall-treated water. The chemical structure and nomenclature of endothall and its monoalkylamine salt are listed in Table A.1. The physicochemical properties of technical grade endothall and its monoalkylamine salt are listed in Table A.2.

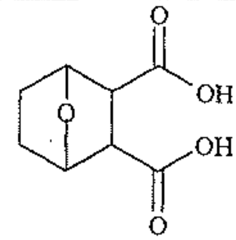
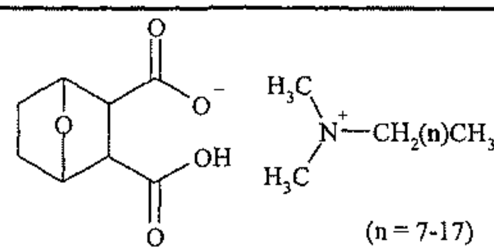
Table A.1. Endothall and Salts Nomenclature	
Chemical Structure	
Common name	Endothall
Molecular Formula	$C_8H_{10}O_5$
Molecular Weight	186.16
IUPAC name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid
CAS name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid
CAS #	145-73-3
PC Code	038901
Current Food/Feed Site Registration	Cotton, hops, potato, alfalfa grown for seed
Chemical Structure	 (n = 7-17)
Common name	Endothall, mono-N,N-dimethylalkyl amine salt
Molecular Formula	Not available
Molecular Weight	Average: 422
IUPAC name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid, compound with N,N-dimethylcocoamine
CAS name	Not available
CAS #	66330-88-9
PC Code	038905
Current Food/Feed Site Registration	Cotton, hops, potato, alfalfa grown for seed, aquatic uses

Table A.2. Physicochemical Properties of Endothall and Salts		
Parameter	Value	Reference
Endothall (acid)		
Melting point	108-110℃	D187593, D187590, and D187588, 5/5/93, K. Dockter
pH	2.7 at 25℃ (1% solution)	D187593, D187590, and D187588, 5/5/93, K. Dockter
Density, bulk density, or specific gravity	0.481 g/cm^3 (bulk) at 25℃	D187593, D187590, and D187588, 5/5/93, K. Dockter
Water solubility at 25℃	109.8 g/L 13.1 g/100 mL in water, pH 5 12.7 g/100 mL in water, pH 7 12.5 g/100 mL in water, pH 9	D166798, 7/2/92, K. Dockter D207011, 9/30/94, F. Toghrol
Solvent solubility at 25℃	3.4 g/100 mL in acetonitrile 2.4 g/100 mL in n-octanol 16.0 g/100 mL in tetrahydrofuran	D207011, 9/30/94, F. Toghrol
Vapor pressure	3.92 x 10^{-5} mm Hg at 24.3℃	D166798, 7/2/92, K. Dockter

Table A.2. Physicochemical Properties of Endothall and Salts		
Parameter	Value	Reference
Dissociation constant, pK_a	4.32 for Step 1 and 6.22 for Step 2 at 20℃ (0.2% solution in 20% basic ethanol); dissociation rate 1.8-2.3 x 10^3 µmho within 3-5 minutes at □25℃, by conductivity meter	D188708, 5/3/93, K. Dockter
Octanol/water partition coefficient	Not applicable to endothall acid	D166798, 7/2/92, K. Dockter
UV/visible absorption spectrum	Not available	
Endothall, mono-N,N-dimethylalkyl amine salt		
Boiling point	Not available	
pH	5.2 at 25℃ (1% solution)	D187593, D187590, and D187588, 5/5/93, K. Dockter
Density, bulk density, or specific gravity	1.028 g/mL at 25℃	D187593, D187590, and D187588, 5/5/93, K. Dockter
Water solubility at 25℃	≥49.2 g/100mL in water, pH 5 ≥51.6 g/100 mL in water, pH 7 ≥49.8 g/100 mL in water, pH 9	D210814, 8/9/95, S. Knizner
Solvent solubility at 25℃	≥102.5 g/100mL in acetonitrile ≥95.4 g/100 mL in n-octanol ≥104.3 g/100 mL in tetrahydrofuran	D210814, 8/9/95, S. Knizner
Vapor pressure	2.09 x 10^{-5} mm Hg at 25℃ (calculated; mixed mono- and dialkylamine (C8-C20))	D206344, 9/22/94, F. Toghrol
Dissociation constant, pK_a	4.24 for Step 1 and 6.07 for Step 2 at 20℃ for mixed mono- and dialkylamine (C8-C20) in acidified ethanol/water; dissociation complete □17 minutes (1.7 x 10^3 µmho) at 25℃	D198885, 4/7/94, F. Toghrol
Octanol/water partition coefficient	K_{OW} 2.097 at concentrations of 8.9 x 10^{-3} M and 8.9 x 10^{-4} M, at 25℃	D209995, 1/20/95, L. Edwards
UV/visible absorption spectrum	Not available	

B. EXPERIMENTAL DESIGN

B.1. Study Site Information

Two onion field trials (one green and one dry bulb) were conducted in Zones 6 and 10 during 2007 (Table B.1.1). The irrigation water used in each test was treated with endothall (2.0 lb ae/gal SC monoalkylamine salt) at a concentration of ~5 ppm, acid equivalent. The treated water was then applied using overhead sprinklers to the onions as six broadcast foliar applications during vegetative development at RTIs of 7-8 days. A volume equivalent to ~1 acre inch of water (~27,000 gal/A) was applied for each application. Based on the concentration of the endothall and the amount of water applied, application rates for endothall were equivalent to 1.12-1.13 lb ae/A/application, for a total of 6.75-6.76 lb ae/A/season (Table B.1.3). These rates are expected to be conservative relative to actual applications.

TABLE B.1.1. Trial Site Conditions.				
Trial Identification (City, State; Year)	Soil characteristics[1]			
	Type	%OM	pH	CEC (meq/g)
East Bernard, TX 2007 TX$07	Clay	0.6	7.3	21.1
Arroyo Grande, CA 2007 CA$18	Sandy Loam	1.2	6.6	8.6

[1]These parameters are optional except in cases where their value affects the use pattern for the chemical.

TABLE B.1.2. Water Characterization.					
Study site	Water characteristics				
	Type	Hardness/Salinity	pH	Turbidity	Dissolved OM
East Bernard, TX 2007 TX$07	Well	NR	NR	NR	NR
Arroyo Grande, CA 2007 CA$18	Well	NR	NR	NR	NR

The actual temperature recordings and rainfall were typical for each site and no unusual weather conditions were reported. Aside from the treated-irrigations, no other irrigation was reported during the study period. The tests were conducted according to normal agricultural practices for the regions, and information was provided on maintenance pesticides and fertilizers used at each site. No information was provided on the characteristics of the water used for irrigation, other than the source (Table B.1.2).

TABLE B.1.3. Study Use Pattern.							
Location (City, State; Year) Trial ID	End-Use Product	Application; no adjuvant used					
		Method; Timing	Concen. (ppm) [1]	Volume (gal/A) [2]	Single Rate (lb ae/A) [3]	RTI [4] (days)	Total Rate (lb ae/A) [3]
East Bernard, TX 2007 TX$07	2.0 lb/gal SC/L	Six broadcast foliar application during vegetative development (BBCH 13-43) using overhead sprinklers.	5.0	27,046-27,132	1.12-1.13	7-8	6.75
Arroyo Grande, CA 2007 CA$18	2.0 lb/gal SC/L	Six broadcast foliar application during vegetative development using overhead sprinklers.	5.0	27,148	1.13	7	6.76

1 The concentration of endothall (in acid equivalents) in the irrigation water. No adjuvants were included in the irrigation water.
2 The target irrigation rate was 1 acre inch of water or 27,154 gal/A.
3 The equivalent field use rates were calculated by the reviewer based on the concentration of the endothall (ae), the application volume and plot size.
4 RTI = Retreatment Interval.

TABLE B.1.4. Trial Numbers and Geographical Locations.

NAFTA Growing Zones	Green Onion			Bulb Onion		
	Submitted	Requested[1]		Submitted	Requested[1]	
		Canada	U.S.		Canada	U.S.
1	--	--	--	--	3	1
1A	--	--	--	--	4	--
2	--	--	--	--	--	--
3	--	--	--	--	--	--
4	--	--	--	--	--	--
5	--	1	--	--	3	1[0]
5A	--	--	--	--	--	--
5B	--	1	--	--	2	--
6	1	--	--	--	--	1
7	--	--	--	--	--	--
7A	--	--	--	--	--	--
8	--	--	--	--	--	1
9	--	--	--	--	--	--
10	--	--	--	1	--	2
11	--	--	--	--	--	1
12	--	--	--	--	1	1[0]
13	--	--	--	--	--	--
Total	1	2	3 [2]	2	5	8[6] [3]

1 Based on EPA OPPTS Guideline 860.1500.
2 Guidelines do not specify zones for green onion trials.
3 The number in brackets indicates a 25% reduction required to support a crop group tolerance.

B.2. Sample Handling and Preparation

Green and bulb onions were harvested at 0 DAT (after the sixth application). A single control and duplicate treated samples of green onion, whole plant without roots (≥4.2 lbs/sample) and bulb onion (≥12 lbs/sample) were collected from each test at 0 DAT and placed in frozen storage at each test facility within 1 hour. Samples were stored frozen at the field sites for 14-28 days. Samples were then shipped by ACDS freezer truck to the analytical laboratory, United Phosphorus, Inc. (King of Prussia, PA), and stored frozen (≤-18EC) prior to analysis.

B.3. Analytical Methodology

Residues of endothall (free acid) in/on onions were determined using a LC/MS/MS method (Method No. KP-242R1) entitled "Analytical Method for Determination of Endothall in Crops", issued 5/4/2007.

For this method, residues were extracted twice by homogenization with water followed by centrifugation and filtering. Residues were then derivatized with HFTH in 50% H_3PO_4 at 100-120°C for 90 minutes. After cooling, the derivatized residues were partitioned into MTBE, evaporated to dryness, and reconstituted in hexane:MTBE (1:1 v:v). Residues were then cleaned using an amine SPE cartridge eluted with methanol:MTBE (1:4). Residues were analyzed by

LC/MS/MS using external standards. The m/z 397→166 ion transition was used for quantifying residues. Residues are expressed in endothall acid equivalents. The validated LOQ for endothall in/on onions is 0.05 ppm. An LOD of 0.00001 ppm was reported; however, this value was the instrument LOD, rather than the LOD of residue in a control matrix.

The above method was validated prior to and in conjunction with the analysis of the onion field trial samples. Control samples of bulb onions were fortified with endothall at 0.05-5.0 ppm for method validation, and control samples of bulb and green onions were fortified with endothall at 0.05 and 0.5 ppm for concurrent recoveries.

C. RESULTS AND DISCUSSION

The LC/MS/MS method used for determining residues of endothall in/on onions was adequately validated prior to and in conjunction with the analysis of field trial samples. The average method validation recoveries (±S.D.) were 83 ± 6% for bulb onion. The average concurrent recoveries (±S.D) were 75 ± 4% for green onion and 90 ± 7% for bulb onion. Apparent residues of endothall were non-detectable in/on control samples of onions. Adequate sample calculations and example chromatograms were provided, and the fortification levels used for the method recoveries were similar in magnitude to the measured residue levels.

Green and bulb onion samples were stored at <-18°C for up to 143 and 63 days, respectively, prior to analysis (Table C.2). Adequate storage stability data are available indicating that endothall is stable in frozen lettuce and sugar beet roots for up to 465 days (47520719.der, under review). The stability data for lettuce and beet roots will support the storage durations and conditions for the current onion field trials.

Following six overhead sprinkler applications with irrigation water containing endothall at 5 ppm (6.75-6.76 lb ae/A/season), endothall residues at 0 DAT were 0.234 and 0.0284 ppm in/on 2 samples of green onions and <0.05 ppm in/on 2 samples of dry bulb onions (Table C.3). The average residues were 0.259 ppm for green onions and <0.05 ppm for dry bulb onions (Table C.4). No residue decline data was provided.

No phytotoxicity was noted on the treated onion crops. Common cultural practices were used to maintain plants, and the weather conditions and maintenance chemicals and fertilizer used in this study did not have a notable impact on the residue data.

TABLE C.1. Summary of Method Validation and Concurrent Recoveries of Endothall from Green and Bulb Onion.

Matrix	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean ± Std. Dev. (%)
Method Validation				
Bulb onion	0.05	3	77, 92, 92	87 ± 9
	0.5	3	85, 76, 79	80 ± 5
	5.0	3	88, 82, 77	82 ± 6
	Total	9	77-92	83 ± 6

TABLE C.1. Summary of Method Validation and Concurrent Recoveries of Endothall from Green and Bulb Onion.

Matrix	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean ± Std. Dev. (%)
Concurrent Recoveries				
Green onion	0.05	1	72	72
	0.5	1	78	78
	Total	**2**	**72-78**	**75 ± 4**
Bulb onion	0.05	1	85	85
	0.5	1	95	95
	Total	**2**	**85-95**	**90 ± 7**

[1] Standard deviations are calculated for data sets having ≥3 values.

TABLE C.2. Summary of Storage Conditions.

Matrix	Storage Temperature (°C)	Actual Storage Duration (days)[1]	Interval of Demonstrated Storage Stability (days) [2]
Green onion	≤-18	143	465
Bulb onion		63	

[1] Interval from harvest to extraction for analysis. Extracts were stored up to 1 day prior to analysis.
[2] Endothall is stable in frozen lettuce and sugar beet roots for up to 467 days (47520719.der under review).

TABLE C.3. Residue Data from Onion Field Trials with Endothall (SC/L).

Trial ID (City, State; Year)	Zone	Crop; Variety	Matrix	Total Rate [1]		PHI (days)	Residues (ppm) [2,3]	
				ppm	lb ae/A			
East Bernard, TX 2007 TX$07	6	Green Onion; Evergreen Hardy White	Whole plant without roots	5.0	6.75	0	0.284	0.234
Arroyo Grande, CA 2007 CA$18	10	Dry Bulb Onion; Onion Yellow Granex F1	Dry Bulb	5.0	6.76	0	(0.023)	(0.023)

[1] The rate is expressed both in terms of the concentration in the irrigation water (ppm) and the total amount (lb ae/A) applied.
[2] Expressed in acid equivalents. The LOQ is 0.05 ppm and the LOD is 0.0001 ppm. Values in parenthesis are >LOD and <LOQ.
[3] The two results for each field trial represent two samples taken from a single plot, not two plots.

TABLE C.4. Summary of Residue Data from Onion Field Trials with Endothall (SC/L). FIX

Commodity	Total Applic. Rate [1]	PHI (days)	Residue Levels (ppm) [2]						
			n	Min.	Max.	HAFT [3]	Median (STMdR)	Mean (STMR)	Std. Dev.
Green Onion	5.0 ppm (6.75)	0	1	0.259	0.259	0.259	0.259	0.259	NA
Dry Bulb onion	5.0 (6.76)	0	1	<0.05	<0.05	<0.05	<0.05	<0.05	NA

[1] The value in parentheses is the total application rate in terms of lb ae/A.
[2] Residues are expressed in terms of the free acid. The LOQ is 0.05 ppm. The LOQ was used for all values reported ≤LOQ.
[3] HAFT = Highest Average Field Trial.

D. CONCLUSION

The available field trial data are adequate and support the use of endothall-treated water for irrigation of onions. The data support the use of endothall in irrigation water at a concentration of 5 ppm (ae), with no more that six applications per season, and a minimum7-day interval between applications to the water. Results are taken at a 0-day PHI.

E. REFERENCES

None

F. DOCUMENT TRACKING

RDI: D. Soderberg (5 June 2009); William Donovan (5 June 2009)
Petition Number: 8E7419
DP#: 356315
PC Code: 038901, 038905

Template Version June 2005

Primary Evaluator	David Soderberg, Chemist, RABV, HED	Date: 5 June 2009
Approved by	William Donovan, Senior Scientist RABV, HED	Date: 5 June 2009

This DER was originally prepared under contract by Dynamac Corporation (1910 Sedwick Road, Building 100, Suite B, Durham, NC 27713; submitted 3/25/2009). The DER has been reviewed by the Health Effects Division (HED) and revised as needed for clarity, correctness and to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORT:

47520703. Arsenovic, M. (2008) Endothall (Hydrothol 191 and Aquathol K): Magnitude of the Residue on Vegetable, Leafy, except Brassica Group: Lab Project Number: Z9757. Unpublished study prepared by Interregional Research Project No. 4. 289 pages.

EXECUTIVE SUMMARY:

Interregional Research Project No. 4 (IR-4) submitted field trial data reflecting the exposure of leaf and head lettuce to endothall through the use of treated irrigation water. Two leaf lettuce field trials and two head lettuce field trials were conducted in Zones 1 and 10 during 2006-2007. Side-by-side tests were conducted in each field trial using irrigation water treated with either the monoalkylamine salt of endothall (2 lb ae/gal SC/L) at a concentration of 5 ppm ae, or the dipotassium salt of endothall (3.0 lb ae/gal SC/L) at a concentration of 3.5 ppm ae. [In order to avoid the complications of different molecular weights for the different salts, endothall concentrations are expressed as the free acid (ae).] The treated water was applied in each test during vegetative development as six broadcast foliar applications using overhead sprinklers, at retreatment intervals (RTIs) of 6-8 days. A volume equivalent to ~1 acre inch of water (~27,000 gal/A) was applied for each application. Based on the endothall concentration and the amount of water applied, the application rates for the monoalkylamine salt of endothall were equivalent to 1.12-1.20 lb ae/A/application, for a total of 6.73-7.17 lb ae/A/season. The application rates for the dipotassium salt were equivalent to 0.78-0.84 lb ae/A/application, for a total of 4.67-5.07 lb ae/A/season.

Single control and duplicate treated samples of leaf lettuce and head lettuce (with wrapper leaves) were harvested from the respective tests on the day of the final application (0 days after treatment, DAT), and samples were stored at <-18°C for up to 92 days prior to analysis. Adequate storage stability data are available to support the duration and conditions of sample storage.

Residues of endothall (free acid) in/on lettuce were determined using an adequate LC/MS/MS method (Method No. KP-242R1). For this method, residues were extracted with water and then derivatized with heptafluoro-*p*-tolylhydrazine (HFTH) in 50% H_3PO_4. The derivatized residues

were cleaned up by partitioning into methyl t-butyl ether (MTBE) and elution through an amine solid phase extraction (SPE) cartridge. Residues were then analyzed by LC/MS/MS using external standards for quantitation. Residues are expressed in endothall acid equivalents. The validated limit of quantitation (LOQ) for endothall in/on lettuce is 0.05 ppm.

Following six overhead sprinkler applications with irrigation water containing the monoalkylamine salt of endothall at 5 ppm ae (6.73-7.17 lb ae/A/season), endothall residues at 0 DAT were 0.410-1.24 ppm ae in/on 4 samples of leaf lettuce and 0.081-0.604 ppm ae in/on 4 samples of head lettuce. Average endothall residues were 0.714 ppm ae for leaf lettuce and 0.317 ppm ae for head lettuce. The highest average field trial (HAFT) residues in/on leaf and head lettuce were 0.992 and 0.548 ppm ae, respectively.

Following six overhead sprinkler applications with irrigation water containing the dipotassium salt of endothall at 3.5 ppm ae (4.67-5.07 lb ae/A/season), endothall residues at 0 DAT were 0.241-1.01 ppm in/on 4 samples of leaf lettuce and <0.05-0.582 ppm in/on 4 samples of head lettuce. Average endothall residues were 0.523 ppm in/on leaf lettuce and 0.288 ppm in/on head lettuce, and HAFT residues in/on leaf and head lettuce were 0.798 and 0.509 ppm, respectively.

Although average endothall residues were lower (0.7-0.9x) for the dipotassium salt than the monoalkylamine salt, direct comparison of the two formulations is not possible as the two formulations were applied at different rates. The monoalkylamine salt was applied at 5 ppm acid equivalents but the dipotassium salt was applied at only 3.5 ppm acid equivalent, 0.7x the rate of the monoalkylamine salt. [Note that these two different application rates are each entirely consistent with different label directions for the two salts. The two labels specify recipes that lead to application of the dipotasium salt at 5 ppm as the salt, and application of the alkylamine salt as 5 ppm as the free acid.]

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the field trial residue data for the monoalkylamine salt of endothall are scientifically acceptable. However, the field trial data for the dipotassium salt were not adequate for comparison with the monoalkylamine salt because the dipotassium was applied at 0.7x the rate of the monoalkylamine salt. Although few trials were performed for each crop, the results of these trials are expected to be conservative. The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document, DP# 356315.

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported which would have an adverse impact on the validity of the study.

A. BACKGROUND INFORMATION

Endothall [7-oxabicyclo[2,2,1] heptane-2,3-dicarboxylic acid] is a selective contact herbicide, defoliant, desiccant, and aquatic algicide that belongs to the dicarboxylic acid chemical class. The free acid of endothall (PC Code 038901) and its dipotassium (PC Code 038904) and alkylamine (PC Code 038905) salts are registered primarily as aquatic herbicides for the control a variety of plants in water bodies. This includes irrigation canals, but only with a 7 day holding period. They are also registered for desiccation/ defoliation of alfalfa/clover (grown for seed only), cotton, and potatoes prior to harvest, and for reduction of sucker branch growth in hops. Permanent tolerances are established for the combined residues of endothall and its monomethyl ester at 0.1 ppm in/on cotton seeds, fish, dried hops and potatoes, and at 0.05 ppm in/on rice grain and straw [40 CFR §180.293(a)(1)].

In conjunction with a petition for tolerances on a wide variety of irrigated crops (PP# 8E7419), IR-4 has submitted field trial data reflecting irrigation of leaf and head lettuce with endothall-treated water. The chemical structure and nomenclature of endothall and its salts are listed in Table A.1. The physicochemical properties of technical grade endothall and its salts are listed in Table A.2.

Table A.1. Structure and Nomenclature of Endothall and its Salts.

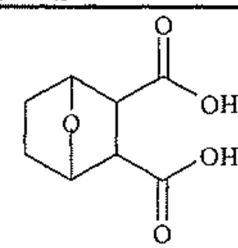
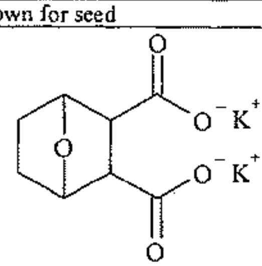
Chemical Structure	
Common name	Endothall
Molecular Formula	$C_8H_{10}O_5$
Molecular Weight	186.16
IUPAC name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid
CAS name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid
CAS #	145-73-3
PC Code	038901
Current Food/Feed Site Registration	Cotton, hops, potato, alfalfa grown for seed
Chemical Structure	
Common name	Endothall, dipotassium salt
Molecular Formula	$C_8H_8K_2O_5$
Molecular Weight	262.33
IUPAC name	Not available
CAS name	Not available
CAS #	2164-07-0
PC Code	038904
Current Food/Feed Site Registration	Cotton, hops, potato, alfalfa grown for seed, aquatic uses

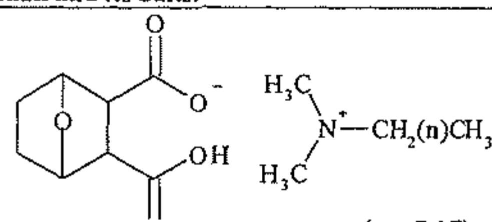
Table A.1. Structure and Nomenclature of Endothall and its Salts.	
Chemical Structure	 (n = 7-17)
Common name	Endothall, mono-N,N-dimethylalkyl amine salt
Molecular Formula	Not available
Molecular Weight	Average: 422
IUPAC name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid, compound with N,N-dimethylcocoamine
CAS name	Not available
CAS #	66330-88-9
PC Code	038905
Current Food/Feed Site Registration	Cotton, hops, potato, alfalfa grown for seed, aquatic uses

Table A.2. Physicochemical Properties of Endothall and Salts.		
Parameter	Value	Reference
Endothall (acid)		
Melting point	108-110°C	D187593, D187590, and D187588, 5/5/93, K. Dockter
pH	2.7 at 25°C (1% solution)	D187593, D187590, and D187588, 5/5/93, K. Dockter
Density, bulk density, or specific gravity	0.481 g/cm^3 (bulk) at 25°C	D187593, D187590, and D187588, 5/5/93, K. Dockter
Water solubility at 25°C	109.8 g/L 13.1 g/100 mL in water, pH 5 12.7 g/100 mL in water, pH 7 12.5 g/100 mL in water, pH 9	D166798, 7/2/92, K. Dockter D207011, 9/30/94, F. Toghrol
Solvent solubility at 25°C	3.4 g/100 mL in acetonitrile 2.4 g/100 mL in n-octanol 16.0 g/100 mL in tetrahydrofuran	D207011, 9/30/94, F. Toghrol
Vapor pressure	3.92 x 10^{-5} mm Hg at 24.3°C	D166798, 7/2/92, K. Dockter
Dissociation constant, pK$_a$	4.32 for Step 1 and 6.22 for Step 2 at 20°C (0.2% solution in 20% basic ethanol); dissociation rate 1.8-2.3 x 10^3 µmho within 3-5 minutes at □25°C, by conductivity meter	D188708, 5/3/93, K. Dockter
Octanol/water partition coefficient	Not applicable to endothall acid	D166798, 7/2/92, K. Dockter
UV/visible absorption spectrum	Not available	
Endothall, dipotassium salt		
Melting point	>360°C	D187593, D187590, and D187588, 5/5/93, K. Dockter
pH	9.1 at 25°C (1% solution)	D187593, D187590, and D187588, 5/5/93, K. Dockter
Density, bulk density, or specific gravity	0.766 g/cm^3 (bulk) at 25°C	D187593, D187590, and D187588, 5/5/93, K. Dockter
Water solubility	>65 g/100 mL in water, pH 5, pH 7, and pH 9	D214691, 6/7/95, D. Hrdy
Solvent solubility	<0.001 g/100 mL in acetonitrile, n-octanol, and tetrahydrofuran	D214691, 6/7/95, D. Hrdy
Vapor pressure	Not applicable. An organic acid K salt is anticipated to have an insignificant vapor pressure.	D178085, 6/18/92, S. Funk

Table A.2. Physicochemical Properties of Endothall and Salts.		
Parameter	Value	Reference
Dissociation constant, pK_a	4.16 for Step 1 and 6.14 for Step 2 at 20℃ in water; dissociation complete at 5 mins (13.6 x 10^3 μmho)	D304027, 6/10/2004, D. Soderberg
Octanol/water partition coefficient	K_{OW} <0.02 and <0.3 at concentrations of 9 x 10^{-3} M and 9 x 10^{-4} M, respectively, at 25℃	D210814, 8/9/95, S. Knizner
UV/visible absorption spectrum	Not available	
Endothall, mono-N,N-dimethylalkyl amine salt		
Boiling point	Not available	
pH	5.2 at 25℃ (1% solution)	D187593, D187590, and D187588, 5/5/93, K. Dockter
Density, bulk density, or specific gravity	1.028 g/mL at 25℃	D187593, D187590, and D187588, 5/5/93, K. Dockter
Water solubility at 25℃	≥49.2 g/100mL in water, pH 5 ≥51.6 g/100 mL in water, pH 7 ≥49.8 g/100 mL in water, pH 9	D210814, 8/9/95, S. Knizner
Solvent solubility at 25℃	≥102.5 g/100mL in acetonitrile ≥95.4 g/100 mL in n-octanol ≥104.3 g/100 mL in tetrahydrofuran	D210814, 8/9/95, S. Knizner
Vapor pressure	2.09 x 10^{-5} mm Hg at 25℃ (calculated; mixed mono- and dialkylamine (C8-C20))	D206344, 9/22/94, F. Toghrol
Dissociation constant, pK_a	4.24 for Step 1 and 6.07 for Step 2 at 20℃ for mixed mono- and dialkylamine (C8-C20) in acidified ethanol/water; dissociation complete □17 minutes (1.7 x 10^3 μmho) at 25℃	D198885, 4/7/94, F. Toghrol
Octanol/water partition coefficient	K_{OW} 2.097 at concentrations of 8.9 x 10^{-3} M and 8.9 x 10^{-4} M, at 25℃	D209995, 1/20/95, L. Edwards
UV/visible absorption spectrum	Not available	

B. EXPERIMENTAL DESIGN

B.1. Study Site Information

Two leaf lettuce field trials and two head lettuce field trials were conducted in Zones 1 and 10 during 2006-2007 (Table B.1.1). Side-by-side tests were conducted in each field trial using irrigation water treated with either the monoalkylamine salt of endothall (2.0 lb ae/gal SC/L) at a concentration of 5 ppm, acid equivalent, or the dipotassium salt of endothall (3.0 lb ae/gal SC/L) at a concentration of 3.5 ppm, acid equivalent. HED notes that although the dipotassium salt was applied at a concentration of ~5 ppm ai, this rate is equivalent to a concentration of 3.5 ppm, acid equivalent. The treated water was applied in each test during vegetative development as six broadcast foliar applications using overhead sprinklers, at RTIs of 6-8 days. A volume equivalent to ~1 acre inch of water (~27,000 gal/A) was applied for each application. Based on the concentration of the endothall and the amount of water applied, the application rates for the monoalkylamine salt of endothall were equivalent to 1.12-1.20 lb ae/A/application, for a total of 6.73-7.17 lb ae/A/season (Table B.1.3). The application rates for the dipotassium salt were equivalent to 0.78-0.84 lb ae/A/application, for a total of 4.67-5.07 lb ae/A/season. These rates are expected to be conservative relative to actual treatment conditions.

TABLE B.1.1. Trial Site Conditions.				
Trial Identification (City, State; Year)	Soil characteristics[1]			
	Type	%OM	pH	CEC (meq/100g)
Arroyo Grande, CA 2006 CA$04	Sandy Loam	1.9	5.7	12.6
Arroyo Grande, CA 2006 CA$05	Sandy Loam	1.9	5.7	12.6
North Rose, NY 2007 NY$28	Loamy Sand	3.02	6.1	5.17
Lyons, NY 2007 NY$31	Sandy Loam	2.7	5.9	6.7

[1]These parameters are optional except in cases where their value affects the use pattern for the chemical.

TABLE B.1.2. Water Characterization.					
Study site	Water characteristics				
	Type	Hardness/Salinity	pH	Turbidity	Dissolved OM
Arroyo Grande, CA 2006 CA$04	Well	NR	NR	NR	NR
Arroyo Grande, CA 2006 CA$05	Well	NR	NR	NR	NR
North Rose, NY 2007 NY$28	Well	NR	NR	NR	NR
Lyons, NY 2007 NY$31	Pond Water	NR	NR	NR	NR

NR = not reported.

The actual temperature recordings and rainfall were typical for each site and no unusual weather conditions were reported. Aside from the treated-irrigations, no other irrigation was reported during the study period. The tests were conducted according to normal agricultural practices for the regions, and information was provided on maintenance pesticides and fertilizers used at each site. No information was provided on the characteristics of the water used for irrigation, other than the source (Table B.1.2).

TABLE B.1.3. Study Use Pattern.

Location (City, State; Year) Trial ID	End-Use Product [1]	Application Information					
		Method; Timing	Concen. (ppm) [2]	Volume (gal/A)	Single Rate (lb ae/A)	RTI[1] (days)	Total Rate (lb ae/A)
Leaf Lettuce							
Arroyo Grande, CA 2006 CA$04	2.0 lb/gal SC	Six overhead sprinkler applications during vegetative development	5.0	27,149	1.13	7	6.76
	3.0 lb/gal SC	Six overhead sprinkler applications during vegetative development	3.5		0.80	7	4.81
North Rose, NY 2007 NY$28	2.0 lb/gal SC	Six overhead sprinkler applications during vegetative development	5.0	26,544	1.12	7	6.73
	3.0 lb/gal SC	Six overhead sprinkler applications during vegetative development	3.5		0.78	7	4.67
Head Lettuce							
Arroyo Grande, CA 2006 CA$05	2.0 lb/gal SC	Six overhead sprinkler applications during vegetative development	5.0	27,149	1.13	6-8	6.76
	3.0 lb/gal SC	Six overhead sprinkler applications during vegetative development	3.5		0.80	6-8	4.81
Lyons, NY 2007 NY$31	2.0 lb/gal SC	Six overhead sprinkler applications during vegetative development	5.0	27,191	1.20	6-8	7.17
	3.0 lb/gal SC	Six overhead sprinkler applications during vegetative development	3.5		0.84	6-8	5.07

1 The two formulations used are expressed in lb acid equivalent/gal. The monoalkylamine salt is a 2.0 lb ae/gal SC/L and the dipotassium salt is a 3.0 lb ae/gal SC/L. When applied according to the label directions, the maximum concentration for endothall (free acid) is 5 ppm for the monoalkylamine salt and 3.5 ppm for the dipotassium salt.

2 The concentration of endothall (in acid equivalents) in the irrigation water. No adjuvants were included in the irrigation water.

3 The target irrigation rate was 1 acre inch of water or 27,154 gal/A.

4 The equivalent field use rates were calculated by the reviewer based on the concentration of the endothall (ae), the application volume and plot size.

4 RTI = Retreatment Interval.

TABLE B.1.4. Trial Numbers and Geographical Locations.						
NAFTA Growing Zones[3]	Head Lettuce			Leaf Lettuce		
	Submitted	Requested[1]		Submitted	Requested[1]	
		Canada	U.S.		Canada	U.S.
1	1	--	1	1	--	1
2	--	--	1	--	--	1
3	--	--	1	--	--	1
4	--	--	--	--	--	--
5	--	--	--	--	--	--
6	--	--	--	--	--	--
7	--	--	--	--	--	--
8	--	--	--	--	--	--
9	--	--	--	--	--	--
10	1	--	6	1	--	6
11	--	--	--	--	--	--
12	--	--	--	--	--	--
13	--	--	--	--	--	--
Total	2	--	8 [6][2]	2	--	8 [6][2]

[1] Based on EPA OPPTS Guideline 860.1500.
[2] The number in brackets indicates a 25% reduction required to support a crop group tolerance.
[3] Zones 1A, 5A and B, 7A and 14-21 were excluded as the proposed use is for the U.S.

B.2. Sample Handling and Preparation

Samples of leaf lettuce and head lettuce (with wrapper leaves) were harvested at 0 DAT. Duplicate control and treated samples (≥2.5 lbs, 12 plants) were collected from each test site and placed in frozen storage at the test facility within 1.5 hours. Samples were stored frozen at the field sites for 4-46 days. Samples were then shipped by ACDS freezer truck to the analytical laboratory, United Phosphorus, Inc. (King of Prussia, PA), and stored at ≤-18EC until analysis.

B.3. Analytical Methodology

Residues of endothall (free acid) in/on lettuce were determined using a LC/MS/MS method (Method No. KP-242R1) entitled "Analytical Method for Determination of Endothall in Crops", issued 5/4/2007.

For this method, residues were extracted twice by homogenization with water followed by centrifugation and filtering. Residues were then derivatized with HFTH in 50% H_3PO_4 at 100-120°C for 90 minutes. After cooling, the derivatized residues were partitioned into MTBE, evaporated to dryness, and reconstituted in hexane:MTBE (1:1 v:v). Residues were then cleaned using an amine SPE cartridge eluted with methanol:MTBE (1:4). Residues were analyzed by LC/MS/MS using external standards. The m/z 397→166 ion transition was used for quantifying residues. Residues are expressed in endothall acid equivalents. The validated LOQ for endothall in/on lettuce is 0.05 ppm, and the LOD was not reported.

The above method was validated prior to and in conjunction with the analysis of the field trial samples. Control samples of lettuce were fortified with endothall at 0.05-5.0 ppm for method validation, and control samples were fortified with endothall at 0.05-2.0 ppm for concurrent recoveries.

C. RESULTS AND DISCUSSION

The LC/MS/MS method used for determining residues of endothall in/on lettuce was adequately validated prior to and in conjunction with the analysis of field trial samples. The average method validation recoveries (±S.D.) were 90 ± 12% and the average concurrent recoveries (±S.D) were 80 ± 9% for lettuce. Apparent residues of endothall were <LOQ in/on control samples of lettuce. Adequate sample calculations and example chromatograms were provided, and the fortification levels used for the method recoveries were similar in magnitude to the measured residue levels.

Lettuce samples were stored at <-18°C for up to 92 days prior to analysis (Table C.2). Adequate storage stability data are available indicating that endothall is stable in frozen lettuce for up to 465 days (47520719.der, under review). These data will support the storage durations and conditions for the current field trials.

Following six overhead sprinkler applications with irrigation water containing the monoalkylamine salt of endothall at 5 ppm, acid equivalents (6.73-7.17 lb ae/A/season), endothall residues at 0 DAT were 0.410-1.24 ppm in/on 4 samples of leaf lettuce and 0.081-0.604 ppm in/on 4 samples of head lettuce (Table C.3). Average endothall residues were 0.714 ppm for leaf lettuce and 0.317 ppm for head lettuce (Table C.4). The HAFT residues in/on leaf and head lettuce were 0.992 and 0.548 ppm, respectively.

Following six overhead sprinkler applications with irrigation water containing the dipotassium salt of endothall at 3.5 ppm, acid equivalents (4.67-5.07 lb ae/A/season), endothall residues at 0 DAT were 0.241-1.01 ppm in/on 4 samples of leaf lettuce and <0.05-0.582 ppm in/on 4 samples of head lettuce. Average endothall residues were 0.523 ppm in/on leaf lettuce and 0.288 ppm in/on head lettuce, and HAFT residues in/on leaf and head lettuce were 0.798 and 0.509 ppm, respectively.

Although average endothall residues were lower (0.7-0.9x) for the dipotassium salt than the monoalkylamine salt, direct comparison of the two formulations is not possible as the two formulations were applied at different rates. The monoalkylamine salt was applied at 5 ppm ae, whereas the dipotassium salt was applied at 5.0 ppm, <u>as the salt</u>, which is 3.5 ppm ae, that is, the dipotassium salt is applied at 0.7x the rate of the monoalkylamine salt. [Note that these two different application rates are each entirely consistent with different label directions for the two salts. The two labels specify recipes that lead to application of the dipotasium salt at 5 ppm as the salt, and application of the alkylamine salt as 5 ppm as the free acid.]

Common cultural practices were used to maintain plants, and the weather conditions and maintenance chemicals and fertilizer used in this study were not likely to have a noticeable impact on the residue data. No phytotoxicity of the treated lettuce was reported.

TABLE C.1. Summary of Method Validation and Concurrent Recoveries of Endothall from Lettuce

Matrix	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean ± Std. Dev. [1] (%)
Method Validation				
Lettuce	0.05	3	109, 96, 83	96 ± 13
	0.5	3	80, 73, 80	78 ± 4
	5.0	3	100, 102, 87	96 ± 8
	Total	**9**	**73-109**	**90 ± 12**
Concurrent Recoveries				
Lettuce	0.05	4	71, 73, 91, 76	78 ± 9
	0.25	1	80	80
	0.5	1	73	73
	1.0	1	92	92
	2.0	1	87	87
	Total	**8**	**71-92**	**80 ± 9**

[1] Standard deviations were calculated only for datasets having ≥3 values.

TABLE C.2. Summary of Storage Conditions.

Matrix	Storage Temperature (°C)	Actual Storage Duration (days)[1]	Interval of Demonstrated Storage Stability (days)[2]
Leaf lettuce	≤-18	91-92	465
Head lettuce		34-85	

[1] Interval from harvest to extraction for analysis. Extracts were stored up to 4 days prior to analysis.
[2] Endothall is stable in frozen lettuce for up to 465 days (47520719.der under review).

TABLE C.3. Residue Data from Lettuce Field Trials with Endothall Salts (SC/L).

Trial ID (City, State; Year)	Zone	Crop; Variety	Matrix	Total Rate [1] ppm	Total Rate [1] lb ae/A	PHI (days)	Residues (ppm) [2,3]	
Leaf Lettuce								
Arroyo Grande, CA 2006 CA$04	10	Leaf lettuce; Greenstar	Leaves	5.0	6.76	0	0.743	1.240
				3.5	4.81	0	0.582	1.013
North Rose, NY 2007 NY$28	1	Leaf Lettuce; Green salad bowl	Leaves	5.0	6.73	0	0.462	0.410
				3.5	4.67	0	0.255	0.241
Head Lettuce								
Arroyo Grande, CA 2006 CA$05	10	Head Lettuce; Snaiper	Heads, w/wrapper leaves	5.0	6.76	0	0.092	0.081
				3.5	4.81	0	<0.05	0.082
Lyons, NY 2007 NY$31	1	Head Lettuce; Ithaca MTO	Heads, w/wrapper leaves	5.0	7.17	0	0.604	0.491
				3.5	5.07	0	0.582	0.436

[1] The rate is expressed both in terms of the concentration in the irrigation water (ppm) and the total amount (lb ae/A) applied. The application concentrations were 5 ppm ae for the monoalkylamine salt and 3.5 ppm ae for the dipotassium salt.
[2] Expressed in endothall acid equivalents. The LOQ is 0.05 ppm.
[3] The two results for each trial are from two samples taken from a single plot, not from two separate plots.

TABLE C.4. Summary of Residue Data from Lettuce Field Trials with Endothall Salts (SC/L).										
Commodity	Formulation type	Total Applic. Rate [1]	PHI (days)	Residue Levels (ppm) [2]						
				N	Min.	Max.	HAFT [3]	Median (STMdR)	Mean (STMR)	Std. Dev.
Leaf lettuce	Monoalkylamine salt (SC/L)	5 ppm (6.73-6.76)	0	2	0.436	.9915	0.9915	0.714	0.714	0.393
	Dipotassium salt (SC/L)	3.5 ppm (4.67-4.81)	0	2	0.248	0.7975	0.7975	0.523	0.523	0.363
Head lettuce	Monoalkylamine salt (SC/L)	5 ppm (6.76-7.17)	0	2	0.0865	0.5475	0.5475	0.292	0.317	0.270
	Dipotassium salt (SC/L)	3.5 ppm (4.81-5.07)	0	2	0.066	0.509	0.509	0.2875	0.2875	0.3132

[1] The concentrations are expressed in acid equivalents, and the values in parentheses are the total application rate in terms of lb ae/A.
[2] Residues are expressed in terms of the free acid. The LOQ is 0.05 ppm.
[3] HAFT = Highest Average Field Trial.

D. CONCLUSION

The available field trial data are adequate and support the use of endothall-treated water for irrigation of lettuce. The data support the use of the monoalkylamine salt of endothall in irrigation water at a concentration of 5 ppm ae and the use of the dipotassium salt of endothall in irrigation water at a concentration of 3.5 ppm ae. No more that six applications of treated water should be made per season, with a minimum 7-day interval between applications to water. Results are determined at a 0-day PHI.

E. REFERENCES

None

F. DOCUMENT TRACKING

RDI: David Soderberg (5 June 2009); William Donovan (5 June 2009)
Petition Number: 8E7419
DP#: 356315
PC Code: 038901, 038904, and 038905

Template Version June 2005

Primary Evaluator	David Soderberg, Chemist, RABV, HED	Date: 5 June 2009
Approved by	William Donovan, Senior Chemist, RABV, HED	Date: 5 June 2009

This DER was originally prepared under contract by Dynamac Corporation (1910 Sedwick Road, Building 100, Suite B, Durham, NC 27713; submitted 3/25/2009). The DER has been reviewed by the Health Effects Division (HED) and revised as needed for clarity, correctness and to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORT:

47520704. Arsenovic, M. (2008) Endothall (Hydrothol 191): Magnitude of the Residue on Vegetable, Brassica Leafy: Lab Project Number: Z9764. Unpublished study prepared by Interregional Research Project No. 4. 149 pages.

EXECUTIVE SUMMARY:

Interregional Research Project No. 4 (IR-4) submitted field trial data reflecting the exposure of cabbage to endothall through the use of treated irrigation water. In two cabbage field trials conducted during 2006 in Zone 1, a 2.0 lb ae/gal soluble concentrate (SC/L) formulation of endothall (monoalkylamine salt) was used to treat the irrigation water at a rate of 5 ppm, acid equivalent (ae). [In order to avoid the complications of different molecular weights for the different salts, endothall concentrations are expressed as the free acid equivalents (ae).] The treated water was applied during vegetative development as six broadcast foliar applications using overhead sprinklers, at retreatment intervals (RTIs) of 6-9 days. Volumes approximating ~1 acre inch of water (27,154 gal/A) were applied for each application. Based on the concentration of the endothall and the actual amount of water applied, the application rates for endothall were equivalent to 0.94 or 1.17 lb ae/A/application, for a total of 5.64 or 7.00 lb ae/A/season.

Single control and duplicate treated samples of cabbages (with wrapper leaves) were harvested from each test on the day of the final application (0 days after treatment, DAT), and samples were stored at <-18°C for up to 118 days prior to analysis. Adequate storage stability data are available to support the duration and conditions of sample storage.

Residues of endothall (free acid) in/on cabbages were determined using an adequate LC/MS/MS method (Method No. KP-242R1). For this method, residues were extracted with water and then derivatized with heptafluoro-*p*-tolylhydrazine (HFTH) in 50% H_3PO_4. The derivatized residues were cleaned up by partitioning into methyl t-butyl ether (MTBE) and elution through an amine solid phase extraction (SPE) cartridge. Residues were then analyzed by LC/MS/MS using external standards for quantitation. Residues are expressed in endothall acid equivalents. The validated limit of quantitation (LOQ) for endothall in/on cabbage is 0.05 ppm.

Following six overhead sprinkler applications with irrigation water containing endothall at 5 ppm (5.64-7.00 lb ae/A/season), endothall residues at 0 DAT were <0.05-0.075 ppm in/on 4 samples of cabbage. The average residues were 0.062 ppm ae and the highest average field trial (HAFT) residues were 0.063 ppm ae. No residue decline data were provided.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the cabbage field trial residue data are scientifically acceptable. Although only two field trials were performed, the results are expected to be conservative relative to actual inadvertent applications. The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document, DP# 356315.

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported which would have an adverse impact on the validity of the study.

A. BACKGROUND INFORMATION

Endothall [7-oxabicyclo[2,2,1] heptane-2,3-dicarboxylic acid] is a selective contact herbicide, defoliant, desiccant, and aquatic algicide that belongs to the dicarboxylic acid chemical class. The free acid of endothall (PC Code 038901) and its dipotassium (PC Code 038904) and alkylamine (PC Code 038905) salts are registered primarily as aquatic herbicides for the control a variety of plants in water bodies. This includes irrigation canals, but only with a 7 day holding period. They are also registered for desiccation/ defoliation of alfalfa/clover (grown for seed only), cotton, and potatoes prior to harvest, and for reduction of sucker branch growth in hops. Permanent tolerances are established for the combined residues of endothall and its monomethyl ester at 0. 1 ppm in/on cotton seeds, fish, dried hops and potatoes, and at 0.05 ppm in/on rice grain and straw [40 CFR §180.293(a)(1)].

In conjunction with a petition for tolerances on a wide variety of irrigated crops (PP# 8E7419), IR-4 has submitted field trial data reflecting irrigation of cabbages with endothall-treated water. The chemical structure and nomenclature of endothall and its monoalkylamine salt are listed in Table A.1. The physicochemical properties of technical grade endothall and its monoalkylamine salt are listed in Table A.2.

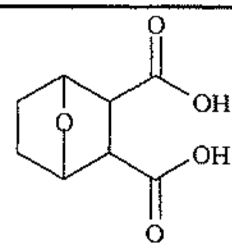
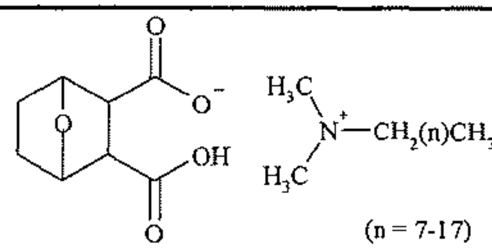
Table A.1. Endothall and Salts Nomenclature	
Chemical Structure	
Common name	Endothall
Molecular Formula	$C_8H_{10}O_5$
Molecular Weight	186.16
IUPAC name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid
CAS name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid
CAS #	145-73-3
PC Code	038901
Current Food/Feed Site Registration	Cotton, hops, potato, alfalfa grown for seed
Chemical Structure	 (n = 7-17)
Common name	Endothall, mono-N,N-dimethylalkyl amine salt
Molecular Formula	Not available
Molecular Weight	Average: 422
IUPAC name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid, compound with N,N-dimethylcocoamine
CAS name	Not available
CAS #	66330-88-9
PC Code	038905
Current Food/Feed Site Registration	Cotton, hops, potato, alfalfa grown for seed, aquatic uses

Table A.2. Physicochemical Properties of Endothall and Salts		
Parameter	Value	Reference
Endothall (acid)		
Melting point	108-110℃	D187593, D187590, and D187588, 5/5/93, K. Dockter
pH	2.7 at 25℃ (1% solution)	D187593, D187590, and D187588, 5/5/93, K. Dockter
Density, bulk density, or specific gravity	0.481 g/cm^3 (bulk) at 25℃	D187593, D187590, and D187588, 5/5/93, K. Dockter
Water solubility at 25℃	109.8 g/L 13.1 g/100 mL in water, pH 5 12.7 g/100 mL in water, pH 7 12.5 g/100 mL in water, pH 9	D166798, 7/2/92, K. Dockter D207011, 9/30/94, F. Toghrol
Solvent solubility at 25℃	3.4 g/100 mL in acetonitrile 2.4 g/100 mL in n-octanol 16.0 g/100 mL in tetrahydrofuran	D207011, 9/30/94, F. Toghrol
Vapor pressure	3.92 x 10^{-5} mm Hg at 24.3℃	D166798, 7/2/92, K. Dockter

Table A.2. Physicochemical Properties of Endothall and Salts

Parameter	Value	Reference
Dissociation constant, pK_a	4.32 for Step 1 and 6.22 for Step 2 at 20°C (0.2% solution in 20% basic ethanol); dissociation rate 1.8-2.3 x 10^3 µmho within 3-5 minutes at □25°C, by conductivity meter	D188708, 5/3/93, K. Dockter
Octanol/water partition coefficient	Not applicable to endothall acid	D166798, 7/2/92, K. Dockter
UV/visible absorption spectrum	Not available	
Endothall, mono-N,N-dimethylalkyl amine salt		
Boiling point	Not available	
pH	5.2 at 25°C (1% solution)	D187593, D187590, and D187588, 5/5/93, K. Dockter
Density, bulk density, or specific gravity	1.028 g/mL at 25°C	D187593, D187590, and D187588, 5/5/93, K. Dockter
Water solubility at 25°C	≥49.2 g/100mL in water, pH 5 ≥51.6 g/100 mL in water, pH 7 ≥49.8 g/100 mL in water, pH 9	D210814, 8/9/95, S. Knizner
Solvent solubility at 25°C	≥102.5 g/100mL in acetonitrile ≥95.4 g/100 mL in n-octanol ≥104.3 g/100 mL in tetrahydrofuran	D210814, 8/9/95, S. Knizner
Vapor pressure	2.09 x 10^{-5} mm Hg at 25°C (calculated; mixed mono- and dialkylamine (C8-C20))	D206344, 9/22/94, F. Toghrol
Dissociation constant, pK_a	4.24 for Step 1 and 6.07 for Step 2 at 20°C for mixed mono- and dialkylamine (C8-C20) in acidified ethanol/water; dissociation complete □17 minutes (1.7 x 10^3 µmho) at 25°C	D198885, 4/7/94, F. Toghrol
Octanol/water partition coefficient	K_{OW} 2.097 at concentrations of 8.9 x 10^{-3} M and 8.9 x 10^{-4} M, at 25°C	D209995, 1/20/95, L. Edwards
UV/visible absorption spectrum	Not available	

B. EXPERIMENTAL DESIGN

B.1. Study Site Information

Two cabbage field trials were conducted in Zone 1during 2007 (Table B.1.1). The irrigation water used in each test was treated with endothall (2.0 lb ae/gal SC monoalkylamine salt) at a concentration of ~5 ppm, acid equivalent. The treated water was then applied to the cabbages during vegetative development as six broadcast foliar applications using overhead sprinklers, at RTIs of 7-8 days. A volume equivalent to ~1 acre inch of water (22,700-28,000 gal/A) was applied for each application. Based on the concentration of the endothall and the actual amount of water applied, application rates for endothall were equivalent to 0.94 or 1.17 lb ae/A/application, for a total of 5.64 or 7.00 lb ae/A/season (Table B.1.3). These rates are expected to be conservative relative to actual applications.

TABLE B.1.1. Trial Site Conditions.

Trial Identification (City, State; Year)	Soil characteristics[1]			
	Type	%OM	pH	CEC (meq/100g)
North Rose, NY 2006 NY$23	Silt Loam	4.7	5.8	8.2
Baptistown, NJ 2006 NJS08	Loam	2.3	6.7	9.1

[1]These parameters are optional except in cases where their value affects the use pattern for the chemical.

TABLE B.1.2. Water Characterization.

Study site	Water characteristics				
	Type	Hardness/Salinity	pH	Turbidity	Dissolved OM
North Rose, NY 2006 NY$23	Well	NR	NR	NR	NR
Baptistown, NJ 2006 NJS08	Well	NR	NR	NR	NR

The actual temperature recordings and rainfall were typical for each site and no unusual weather conditions were reported. No irrigation was reported during the study period. The tests were conducted according to normal agricultural practices for the regions, and information was provided on maintenance pesticides and fertilizers used at each site. No information was provided on the characteristics of the water used for irrigation, other than the source (Table B.1.2).

TABLE B.1.3. Study Use Pattern.

Location (City, State; Year) Trial ID	End-Use Product [1]	Application Information					
		Method; Timing	Concen. (ppm) [2]	Volume (gal/A) [3]	Single Rate (lb ae/A) [4]	RTI [5] (days)	Total Rate (lb ae/A) [4]
North Rose, NY 2006 NY$23	2.0 lb/gal SC/L	Six broadcast foliar application during vegetative development using overhead sprinklers.	4.99	28,032	1.17	7	7.00
Baptistown, NJ 2006 NJ$08	2.0 lb/gal SC/L	Six broadcast foliar application during vegetative development using overhead sprinklers.	4.96-4.97	22,706	0.94	6-9	5.64

[1] The endothall formulation was a monoalkylamine salt containing 2. 0 lb ae/gal.
[2] The concentration of endothall (in acid equivalents) in the irrigation water. No adjuvants were included in the irrigation water.
[3] The target irrigation rate was 1 acre inch of water or 27,154 gal/A. In the NJ field trial, the application volume was determined as inches per acre.
[4] The equivalent field use rates were calculated by the reviewer based on the concentration of the endothall (ae), the application volume and plot size.
[5] RTI = Retreatment Interval.

TABLE B.1.4. Trial Numbers and Geographical Locations.			
NAFTA Growing Zones	Cabbage		
	Submitted	Requested[1]	
		Canada	U.S.
1	2	--	2
1A	--	--	--
2	--	--	1
3	--	--	1
4	--	--	--
5	--	2	1
5A	--	--	--
5B	--	2	--
6	--	--	1
7	--	--	--
7A	--	--	--
8	--	--	1
9	--	--	--
10	--	--	1
11	--	--	--
12	--	1	--
13	--	--	--
Total	2	5	8 [6][2]

1 Based on EPA OPPTS Guideline 860.1500.
2 The number in brackets indicates a 25% reduction required to support a crop group tolerance.

B.2. Sample Handling and Preparation

Cabbages ere harvested at 0 DAT (after the sixth application). A single control and duplicate treated samples of cabbage head with wrapper leaves (≥4 lbs/sample) were collected from each test and placed in frozen storage at each test facility within 1.5 hours. Samples were stored frozen at the field sites for 8-29 days. Samples were then shipped by ACDS freezer truck to the analytical laboratory, United Phosphorus, Inc. (King of Prussia, PA), and stored at ≤-18EC until analysis.

B.3. Analytical Methodology

Residues of endothall (free acid) in/on cabbages were determined using a LC/MS/MS method (Method No. KP-242R1) entitled "Analytical Method for Determination of Endothall in Crops", issued 5/4/2007.

For this method, residues were extracted twice by homogenization with water followed by centrifugation and filtering. Residues were then derivatized with HFTH in 50% H_3PO_4 at 100-120°C for 90 minutes. After cooling, the derivatized residues were partitioned into MTBE, evaporated to dryness, and reconstituted in hexane:MTBE (1:1 v:v). Residues were then cleaned using an amine SPE cartridge eluted with methanol:MTBE (1:4). Residues were analyzed by LC/MS/MS using external standards. The m/z 397→166 ion transition was used for quantifying residues. Residues are expressed in endothall acid equivalents. The validated LOQ for endothall in/on cabbage is 0.05 ppm, and the LOD was estimated to be 0.002 ppm.

The above method was validated prior to and in conjunction with the analysis of the field trial samples. Control samples of cabbage were fortified with endothall at 0.05-5.0 ppm for method validation, and control samples were fortified with endothall at 0.05 and 1.0 ppm for concurrent recoveries.

C. RESULTS AND DISCUSSION

The LC/MS/MS method used for determining residues of endothall in/on cabbage was adequately validated prior to and in conjunction with the analysis of field trial samples. The average method validation recoveries (±S.D.) were 93 ± 10% and the average concurrent recoveries (±S.D) were 93 ± 6% for cabbage. Apparent residues of endothall were <LOQ in/on control samples of cabbage. Adequate sample calculations and example chromatograms were provided, and the fortification levels used for the method recoveries were similar in magnitude to the measured residue levels.

Cabbage samples were stored at <-18°C for up to 118 days prior to analysis (Table C.2). Adequate storage stability data are available indicating that endothall is stable in frozen lettuce for up to 465 days (47520719.der, under review). The stability data for lettuce will support the storage durations and conditions for the current field trials.

Following six overhead sprinkler applications with irrigation water containing endothall at 5 ppm (5.64-7.00 lb ae/A/season), endothall residues at 0 DAT were <0.05-0.75 ppm in/on 4 samples of cabbage (Table C.3). The average residues were 0.062 ppm and the HAFT residues were 0.063 ppm for cabbage (Table C.4). No residue decline data were provided.

Common cultural practices were used to maintain plants, and the weather conditions and maintenance chemicals and fertilizer used in this study were not likely to have had a notable impact on the residue data. No phytotoxicity was noted on the treated cabbage crops.

TABLE C.1. Summary of Method Validation and Concurrent Recoveries of Endothall from Cabbage.

Matrix	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean ± Std. Dev. (%)
Method Validation				
Cabbage, head with wrapper leaves	0.05	3	108, 81, 105	98 ± 15
	0.5	3	91, 100, 90	94 ± 6
	5.0	3	80, 89, 90	86 ± 6
	Total	9	80-108	93 ± 10
Concurrent Recoveries				
Cabbage, head with wrapper leaves	0.05	1	97	97
	0.5	1	88	88
	Total	2	88-97	93 ± 6

[1] Standard deviations are calculated for data sets having ≥3 values.

TABLE C.2. Summary of Storage Conditions.			
Matrix	Storage Temperature (°C)	Actual Storage Duration (days)[1]	Interval of Demonstrated Storage Stability (days)[2]
Cabbage	≤-18	61-118	465

[1] Interval from harvest to extraction for analysis. Extracts were stored up to 1 day prior to analysis.
[2] Endothall is stable in frozen lettuce for up to 465 days (47520719.der under review).

TABLE C.3. Residue Data from Cabbage Field Trials with Endothall (SC/L).								
Trial ID (City, State; Year)	Zone	Variety	Matrix	Total Rate [1]		PHI (days)	Residues (ppm)[1, 3]	
				ppm	lb ae/A			
North Rose, NY 2006 NY$23	1	Matsumo	Head with wrapper leaves	5.0	7.00	0	ND	0.075
Baptistown, NJ 2006 NJ$08	1	Blue Lagoon	Head with wrapper leaves	5.0	5.64	0	0.065	0.058

[1] The rate is expressed both in terms of the concentration in the irrigation water (ppm) and the total amount (lb ae/A) applied.
[2] Expressed as the free acid. The LOQ is 0.05 ppm and the estimated LOD is 0.002 ppm.
3. The two residues for each field trial represent two samples from a single plot, not two plots.

TABLE C.4. Summary of Residue Data from Cabbage Field Trials with Endothall (SC/L).									
Commodity	Total Applic. Rate [1]	PHI (days)	Residue Levels (ppm)[2]						
			N	Min.	Max.	HAFT [1]	Median (STMdR)	Mean (STMR)	Std. Dev.
Cabbage, head with wrapper leaves	5 ppm (5.64-7.00)	0	2	0.0615	0.0625	0.0625	0.062	0.062	0.0007

[1] The value in parentheses is the total application rate in terms of lb ae/A.
[2] Residues are expressed in terms of the free acid. The LOQ is 0.05 ppm. The LOQ was used for all values reported ≤LOQ.
[3] HAFT = Highest Average Field Trial.

D. CONCLUSION

The available field trial data are adequate and support the use of endothall-treated water for irrigation of cabbages. The data support the use of endothall in irrigation water at a concentration of 5 ppm (ae), with no more that six applications per season, and a minimum 7-day interval between applications to the water. Residues in onions are at a 0-day PHI.

E. REFERENCES

None

F. DOCUMENT TRACKING

RDI: David Soderberg (5 June 2009); Will8iam Donovan (5 June 2009)
Petition Number: 8E7419
DP#: 356315
PC Code: 038901 and 038905

Template Version June 2005

Primary Evaluator	David Soderberg, Chemist, RABV, HED	Date: 5 June 2009
Approved by	William Donovan, Senior Scientist, RABV, HED	Date: 5 June 2009

This DER was originally prepared under contract by Dynamac Corporation (1910 Sedwick Road, Building 100, Suite B, Durham, NC 27713; submitted 3/27/2006). The DER has been reviewed by the Health Effects Division (HED) and revised as needed for clarity, correctness and to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORT:

47520707. Arsenovic, M. (2008) Endothall (Hydrothol 191): Magnitude of the Residue on Vegetable, Cucurbit Group: Lab Project Number: Z9755, Z9755.07-ALS01, Unpublished study prepared by Interregional Research Project No. 4. 215 pages.

EXECUTIVE SUMMARY:

Interregional Research Project No. 4 (IR-4) submitted field trial data reflecting the exposure of cucumbers to endothall through the use of treated irrigation water. Two cucumber field trials were conducted in Zones 1 and 5 during 2006-2007. In each trial, side-by-side tests were conducted using irrigation water treated with either the monoalkylamine salt of endothall (2 lb ae/gal SC/L) at a concentration of 5 ppm ae, or the dipotassium salt of endothall (3.0 lb ae/gal SC/L) at a concentration of 3.5 ppm ae. [In order to avoid the complications of different molecular weights for different salts, endothall concentrations are expressed as the free acid equivalents (ae).] The treated water was applied in each test during flowering and fruit development as six broadcast foliar applications using overhead sprinklers, at retreatment intervals (RTIs) of 6-8 days. A volume equivalent to ~1 acre inch of water (~27,000 gal/A) was applied for each application. Based on the endothall concentration and the amount of water applied, the application rate for the monoalkylamine salt of endothall was equivalent to 1.13 lb ae/A/application, for a total of 6.75-6.77 lb ae/A/season. The application rate for the dipotassium salt was equivalent to 0.80 lb ae/A/application, for a total of 4.80-4.81 lb ae/A/season.

Single control and duplicate treated samples of cucumber were harvested from each test on the day of the final application (0 days after treatment, DAT), and samples were stored at ≤-10°C for up to 478 days prior to analysis. Adequate storage stability data are available to support the duration and conditions of sample storage.

Residues of endothall (free acid) in/on cucumbers were determined using an adequate LC/MS/MS method (Method No. KP-242R1). For this method, residues were extracted with water and then derivatized with heptafluoro-*p*-tolylhydrazine (HFTH) in 50% H_3PO_4. The derivatized residues were cleaned up by partitioning into methyl t-butyl ether (MTBE) and elution through an amine solid phase extraction (SPE) cartridge. Residues were then analyzed

by LC/MS/MS using external standards for quantitation. Residues are expressed in endothall acid equivalents. The validated limit of quantitation (LOQ) for endothall in/on cucumbers is 0.05 ppm.

Endothall residues were 0.234-0.738 ppm in/on 4 cucumber samples harvested at 0 DAT following irrigation applications of the monoalkylamine salt of endothall at 5 ppm ae, and were 0.310-0.459 ppm in/on 4 cucumber samples harvested at 0 DAT following six irrigation applications of the dipotassium salt of endothall at 3.5 ppm. Average endothall residues in/on cucumbers were 0.499 and 0.385 ppm for the monoalkylamine and dipotassium salt formulations, respectively. The highest average field trial (HAFT) residues were 0.738 and 0.433 ppm for the monoalkylamine and dipotassium salt formulations, respectively.

Although average endothall residues were lower (0.8x) for the dipotassium salt than the monoalkylamine salt, direct comparison of the two formulations is not possible as the two formulations were applied at different rates. The monoalkylamine salt was applied at 5 ppm ae; however, the dipotassium salt was applied at only 3.5 ppm acid equivalent, 0.7x the rate of the monoalkylamine salt. [Note that these two different application rates are each entirely consistent with different label directions for the two salts. The two labels specify recipes that lead to application of the dipotasium salt at 5 ppm as the salt, and application of the alkylamine salt as 5 ppm as the free acid.]

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the cucumber field trial residue data for the monoalkylamine salt formulation are scientifically acceptable. However, the field trial data for the dipotassium salt are not appropriate for direct comparison with the monoalkylamine salt because the dipotassium was applied at 0.7x the rate of the monoalkylamine salt. Although limited field trials were performed, these applications are expected to be conservative relative to actual inadvertent applications. The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document, DP# 356315.

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported which would have an adverse impact on the validity of the study.

A. BACKGROUND INFORMATION

Endothall [7-oxabicyclo[2,2,1] heptane-2,3-dicarboxylic acid] is a selective contact herbicide, defoliant, desiccant, and aquatic algaecide that belongs to the dicarboxylic acid chemical class. The free acid of endothall (PC Code 038901) and its dipotassium (PC Code 038904) and alkylamine (PC Code 038905) salts are registered primarily as aquatic herbicides for the control a variety of plants in water bodies. This includes irrigation canals, but only with a 7 day holding period. They are also registered for desiccation/ defoliation of alfalfa/clover (grown for seed only), cotton, and potatoes prior to harvest, and for reduction of sucker branch growth in hops. Permanent tolerances are established for the combined residues of endothall and its monomethyl ester at 0.1 ppm in/on cotton seeds, fish, dried hops and potatoes, and at 0.05 ppm in/on rice grain and straw [40 CFR §180.293(a)(1)].

In conjunction with a petition for tolerances on a wide variety of irrigated crops (PP# 8E7419), IR-4 has submitted field trial data reflecting irrigation of cucumbers with endothall-treated water. The chemical structure and nomenclature of endothall and its salts are listed in Table A.1. The physicochemical properties of technical grade endothall and its salts are listed in Table A.2.

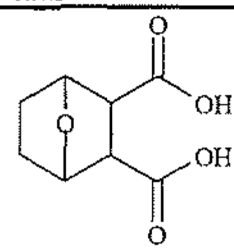
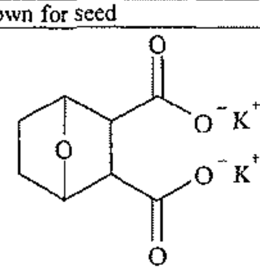
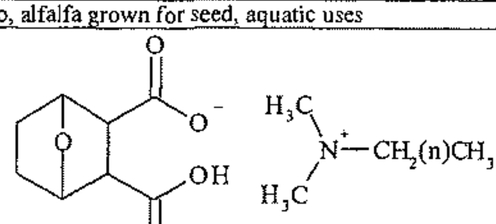
Table A.1. Structure and Nomenclature of Endothall and its Salts.	
Chemical Structure	
Common name	Endothall
Molecular Formula	$C_8H_{10}O_5$
Molecular Weight	186.16
IUPAC name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid
CAS name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid
CAS #	145-73-3
PC Code	038901
Current Food/Feed Site Registration	Cotton, hops, potato, alfalfa grown for seed
Chemical Structure	
Common name	Endothall, dipotassium salt
Molecular Formula	$C_8H_8K_2O_5$
Molecular Weight	262.33
IUPAC name	Not available
CAS name	Not available
CAS #	2164-07-0
PC Code	038904
Current Food/Feed Site Registration	Cotton, hops, potato, alfalfa grown for seed, aquatic uses
Chemical Structure	 (n = 7-17)
Common name	Endothall, mono-N,N-dimethylalkyl amine salt

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Table A.1. Structure and Nomenclature of Endothall and its Salts.	
Molecular Formula	Not available
Molecular Weight	Average: 422
IUPAC name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid, compound with N,N-dimethylcocoamine
CAS name	Not available
CAS #	66330-88-9
PC Code	038905
Current Food/Feed Site Registration	Cotton, hops, potato, alfalfa grown for seed, aquatic uses

Table A.2. Physicochemical Properties of Endothall and Salts.		
Parameter	Value	Reference
Endothall (acid)		
Melting point	108-110℃	D187593, D187590, and D187588, 5/5/93, K. Dockter
pH	2.7 at 25℃ (1% solution)	D187593, D187590, and D187588, 5/5/93, K. Dockter
Density, bulk density, or specific gravity	0.481 g/cm^3 (bulk) at 25℃	D187593, D187590, and D187588, 5/5/93, K. Dockter
Water solubility at 25℃	109.8 g/L 13.1 g/100 mL in water, pH 5 12.7 g/100 mL in water, pH 7 12.5 g/100 mL in water, pH 9	D166798, 7/2/92, K. Dockter D207011, 9/30/94, F. Toghrol
Solvent solubility at 25℃	3.4 g/100 mL in acetonitrile 2.4 g/100 mL in n-octanol 16.0 g/100 mL in tetrahydrofuran	D207011, 9/30/94, F. Toghrol
Vapor pressure	3.92 x 10^{-5} mm Hg at 24.3℃	D166798, 7/2/92, K. Dockter
Dissociation constant, pK_a	4.32 for Step 1 and 6.22 for Step 2 at 20℃ (0.2% solution in 20% basic ethanol); dissociation rate 1.8-2.3 x 10^3 µmho within 3-5 minutes at □25℃, by conductivity meter	D188708, 5/3/93, K. Dockter
Octanol/water partition coefficient	Not applicable to endothall acid	D166798, 7/2/92, K. Dockter
UV/visible absorption spectrum	Not available	
Endothall, dipotassium salt		
Melting point	>360℃	D187593, D187590, and D187588, 5/5/93, K. Dockter
pH	9.1 at 25℃ (1% solution)	D187593, D187590, and D187588, 5/5/93, K. Dockter
Density, bulk density, or specific gravity	0.766 g/cm^3 (bulk) at 25℃	D187593, D187590, and D187588, 5/5/93, K. Dockter
Water solubility	>65 g/100 mL in water, pH 5, pH 7, and pH 9	D214691, 6/7/95, D. Hrdy
Solvent solubility	<0.001 g/100 mL in acetonitrile, n-octanol, and tetrahydrofuran	D214691, 6/7/95, D. Hrdy
Vapor pressure	Not applicable. An organic acid K salt is anticipated to have an insignificant vapor pressure.	D178085, 6/18/92, S. Funk
Dissociation constant, pK_a	4.16 for Step 1 and 6.14 for Step 2 at 20℃ in water; dissociation complete at 5 mins (13.6 x 10^3 µmho)	D304027, 6/10/2004, D. Soderberg
Octanol/water partition coefficient	K_{OW} <0.02 and <0.3 at concentrations of 9 x 10^{-3} M and 9 x 10^{-4} M, respectively, at 25℃	D210814, 8/9/95, S. Knizner
UV/visible absorption spectrum	Not available	
Endothall, mono-N,N-dimethylalkyl amine salt		
Boiling point	Not available	
pH	5.2 at 25℃ (1% solution)	D187593, D187590, and D187588, 5/5/93, K. Dockter

Table A.2. Physicochemical Properties of Endothall and Salts.		
Parameter	Value	Reference
Density, bulk density, or specific gravity	1.028 g/mL at 25°C	D187593, D187590, and D187588, 5/5/93, K. Dockter
Water solubility at 25°C	≥49.2 g/100mL in water, pH 5 ≥51.6 g/100 mL in water, pH 7 ≥49.8 g/100 mL in water, pH 9	D210814, 8/9/95, S. Knizner
Solvent solubility at 25°C	≥102.5 g/100mL in acetonitrile ≥95.4 g/100 mL in n-octanol ≥104.3 g/100 mL in tetrahydrofuran	D210814, 8/9/95, S. Knizner
Vapor pressure	2.09×10^{-5} mm Hg at 25°C (calculated; mixed mono- and dialkylamine (C8-C20))	D206344, 9/22/94, F. Toghrol
Dissociation constant, pK_a	4.24 for Step 1 and 6.07 for Step 2 at 20°C for mixed mono- and dialkylamine (C8-C20) in acidified ethanol/water; dissociation complete □17 minutes (1.7×10^3 µmho) at 25°C	D198885, 4/7/94, F. Toghrol
Octanol/water partition coefficient	K_{OW} 2.097 at concentrations of 8.9×10^{-3} M and 8.9×10^{-4} M, at 25°C	D209995, 1/20/95, L. Edwards
UV/visible absorption spectrum	Not available	

B. EXPERIMENTAL DESIGN

B.1. Study Site Information

Two cucumber field trials were conducted in Zones 1 and 5 during the 2006 and 2007 growing seasons (Table B.1.1). At each site, side-by-side tests were conducted using irrigation water treated with either the monoalkylamine salt of endothall (2.0 lb ae/gal SC/L) at a concentration of 5 ppm, acid equivalent, or the dipotassium salt of endothall (3.0 lb ae/gal SC/L) at a concentration of 3.5 ppm, acid equivalent. HED notes that although the dipotassium salt was applied at a concentration of ~5 ppm ai, this rate is equivalent to a concentration of 3.5 ppm, acid equivalent. The treated water was applied in each test during flowering and fruit development as six broadcast foliar applications using overhead sprinklers, at RTIs of 6-8 days. A volume equivalent to ~1 acre inch of water (~27,000 gal/A) was applied for each application. Based on the concentration of the endothall and the amount of water applied, the application rates for the monoalkylamine salt of endothall were equivalent to 1.13 lb ae/A/application, for a total of 6.75-6.77 lb ae/A/season (Table B.1.3). The application rates for the dipotassium salt were equivalent to 0.80 lb ae/A/application, for a total of 4.80-4.81 lb ae/A/season. These applications are expected to be conservative relative to actual applications.

TABLE B.1.1. Trial Site Conditions.				
Trial Identification (City, State; Year)	Soil characteristics[1]			
	Type	%OM	pH	CEC (meq/100g)
Baptistown, NJ 2006 NJ$02	Loam	2.3	6.7	9.1
Conklin, MI 2007 MI$42	Loam	1.8	6.4	7.6

[1]These parameters are optional except in cases where their value affects the use pattern for the chemical.

TABLE B.1.2. Water Characterization.					
Study site	Water characteristics				
	Type	Hardness/Salinity	pH	Turbidity	Dissolved OM
Baptistown, NJ 2006 NJ$02	Well	NR	NR	NR	NR
Conklin, MI 2007 MI$42	Well	NR	NR	NR	NR

NR= not reported.

The actual temperature recordings and rainfall were typical for each site and no unusual weather conditions were reported. No additional irrigation was reported during the study period. The tests were conducted according to normal agricultural practices for the regions, and information was provided on maintenance pesticides and fertilizers used at each site. No information was provided on the characteristics of the water used for irrigation, other than the source (Table B.1.2).

TABLE B.1.3. Study Use Pattern.							
Location (City, State; Year) Trial ID	End-Use Product [1]	Application Information					
		Method; Timing	Concen. [2]	Volume (gal/A) [3]	Single Rate [4] (lb ae/A)	RTI [5] (days)	Total Rate [4] (lb ae/A)
Baptistown, NJ 2006 NJ$02	2.0 lb/gal SC	Six overhead sprinkler applications during flowering and fruit development	5.0	27,170	1.13	6-8	6.75
	3.0 lb/gal SC	Six overhead sprinkler applications during flowering and fruit development	3.5	27,170	0.80	6-8	4.80
Conklin, MI 2007 MI$42	2.0 lb/gal SC	Six overhead sprinkler applications during flowering and fruit development	5.0	27,154-27,162	1.13	7	6.77
	3.0 lb/gal SC	Six overhead sprinkler applications during flowering and fruit development	3.5	27,152-27,163	0.80	7	4.81

[1] The two formulations used are expressed in lb acid equivalent/gal. The monoalkylamine salt is a 2.0 lb ae/gal SC/L and the dipotassium salt is a 3.0 lb ae/gal SC/L. When applied according to the label directions, the maximum concentration for endothall (free acid) is 5 ppm for the monoalkylamine salt and 3.5 ppm for the dipotassium salt.
[2] The concentration of endothall (in acid equivalents) in the irrigation water. No adjuvants were included in the irrigation water.
[3] The target irrigation rate was 1 acre inch of water or 27,154 gal/A.
[4] The equivalent field use rates were calculated by the reviewer based on the concentration of the endothall (ae), the application volume and plot size.
[5] RTI = Retreatment Interval.

TABLE B.1.4. Trial Numbers and Geographical Locations.

NAFTA Growing Zones[3]	Cucumber		
	Submitted	Requested[1]	
		Canada	U.S.
1	1	--	--
2	--	--	3
3	--	--	1
4	--	--	--
5	1	--	2
6	--	--	1
7	--	--	--
8	--	--	--
9	--	--	--
10	--	--	1
11	--	--	--
12	--	--	--
13	--	--	--
Total	2	--	8[6][2]

1 Based on EPA OPPTS Guideline 860.1500.
2 The number in brackets indicates a 25% reduction required to support a crop group tolerance.
3 ones 1A, 5 A and B, 7A and 14-21 were not included as the proposed use is for the U.S. only

B.2. Sample Handling and Preparation

Duplicate control and treated samples (≥4 lb/sample, 12-24 fruits) of cucumbers were harvested at 0 DAT (after the sixth application) and placed in frozen storage at the test facility within 5.2 hours. Samples were stored frozen at the field sites for 4-29 days prior to shipment by ACDS Freezer truck to the analytical laboratory, ALS Laboratory Group (Edmonton, AB, Canada) where they were stored at ≤-10°C until analysis.

B.3. Analytical Methodology

Residues of endothall (free acid) in/on cucumbers were determined using a LC/MS/MS method (Method No. KP-242R1) entitled "Analytical Method for Determination of Endothall in Crops", issued 5/4/2007.

For this method, residues were extracted twice by homogenization with water followed by centrifugation and filtering. Residues were then derivatized with HFTH in 50% H_3PO_4 at 100-120°C for 90 minutes. After cooling, the derivatized residues were partitioned into MTBE, evaporated to dryness, and reconstituted in hexane:MTBE (1:1 v:v). Residues were then cleaned using an amine SPE cartridge eluted with methanol. Residues were analyzed by LC/MS/MS using external standards. The m/z 397→166 ion transition was used for quantifying residues. Residues are expressed in endothall acid equivalents. The validated LOQ for endothall in/on cucumbers is 0.05 ppm, and the estimated LOD was 0.0025 ppm.

The above method was validated prior to and in conjunction with the analysis of the field trial samples. Control samples of peaches were fortified with endothall at 0.05-5.0 ppm for method validation and at 0.05-1.0 ppm for concurrent recoveries.

C. RESULTS AND DISCUSSION

The LC/MS/MS method used for determining residues of endothall in/on cucumbers was adequately validated prior to and in conjunction with the analysis of field trial samples. Method validation recoveries averaged 114% with a standard deviation of 8%, and concurrent recoveries averaged 92% with a standard deviation of 5% (Table C.1). Apparent residues of endothall were <LOQ in/on all control samples. Adequate sample calculations and example chromatograms were provided, and the fortification levels used for method recoveries were similar in magnitude to the measured residue levels.

Cucumber samples were stored frozen at ≤-10°C for up to 478 days prior to analysis (Table C.2). Adequate storage stability data are available indicating that endothall is stable in frozen tomatoes for up to 467 days (47520719.der, under review). These data will support the storage durations and conditions for the current field trials.

Following six overhead sprinkler applications with irrigation water containing the monoalkylamine salt of endothall at 5 ppm, acid equivalents (6.76-6.77 lb ae/A/season), endothall residues were 0.234-0.738 ppm in/on 4 samples of cucumbers harvested at 0 DAT (Table C.3). Average endothall residues were 0.499 ppm, and the HAFT residues were 0.738 ppm (Table C.4).

Following six overhead sprinkler applications with irrigation water containing the dipotassium salt of endothall at 3.5 ppm, acid equivalents (4.80-4.81 lb ae/A/season), endothall residues were 0.310-0.459 ppm in/on 4 samples of cucumber harvested at 0 DAT. Average endothall residues were 0.385 ppm, and the HAFT residues were 0.433 ppm. No residue decline data was provided.

Although average endothall residues were lower (0.8x) for the dipotassium salt than the monoalkylamine salt, direct comparison of the two formulations is not appropriate because the two formulations were applied at different rates. The monoalkylamine salt was applied at 5 ppm acid equivalents; however, the dipotassium salt was applied at only 3.5 ppm acid equivalent, 0.7x the rate of the monoalkylamine salt. Although the dipotassium salt of endothall was applied according to label directions, using a concentration of 5 ppm ai for the irrigation water, this application rate did not take into account the acid equivalency of the dipotassium salt.

Common cultural practices were used to maintain plants, and the weather conditions and maintenance chemicals and fertilizer used in this study did not have a notable impact on the residue data. Phytotoxicity was reported in the NJ test and included loss of older leaves, stunting of growing tips, cupping of young leaves, chlorosis, and cessation of flowering. However, fruit set and growth were not effected.

TABLE C.1. Summary of Method Validation and Concurrent Recoveries of Endothall from Cucumber.				
Matrix	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean ± Std. Dev. [1] (%)
Method Validation				
Fruit	0.05	3	110, 119, 111	113 ± 5
	0.5	3	96, 117, 118	110 ± 13
	5.0	3	116, 117, 119	117 ± 2
	Total	9	96-119	**114 ± 8**
Concurrent Recoveries				
Fruit	0.05	1	99	99
	0.5	1	96	96
	1.0	3	87, 88, 92	89 ± 3
	Total	5	87-99	92 ± 5

[1] Standard deviations were calculated only for datasets having ≥3 values.

TABLE C.2. Summary of Storage Conditions.			
Matrix	Storage Temperature (°C)	Actual Storage Duration (days)[1]	Interval of Demonstrated Storage Stability (days)[2]
Cucumber	≤-10	478	467

[1] Interval from harvest to extraction for analysis. Extracts were stored up to 5 days prior to analysis.
[2] Endothall is stable in frozen tomatoes for up to 467 days (47520719.der under review).

TABLE C.3. Residue Data from Cucumber Field Trials with Endothall Salts (SC/L).								
Trial ID (City, State; Year)	Zone	Variety	Matrix	Total Rate [1]		PHI (days)	Residues (ppm) [2, 3]	
				ppm	lb ae/A			
Baptistown, NJ 2006 NJ$02	1	Burpless bush	Fruit	5.0	6.75	0	0.738	0.738
				3.5	4.80	0	0.406	0.459
Conklin, MI 2007 MI$42	5	Fancipack	Fruit	5.0	6.77	0	0.234	0.284
				3.5	4.81	0	0.337	0.310

[1] The rate is expressed both in terms of the concentration in the irrigation water (ppm) and the total amount (lb ae/A) applied. The application concentrations were 5 ppm ae for the monoalkylamine salt and 3.5 ppm ae for the dipotassium salt.
[2] Expressed in endothall acid equivalents. The LOQ is 0.05 ppm.
[3] The two results for each field trial represent two samples taken from a single plot, not two plots.

TABLE C.4. Summary of Residue Data from Cucumber Field Trials with Endothall Salts (SC/L).										
Commodity	End-Use Products	Total Applic. Rate [1]	PHI (days)	Residue Levels (ppm) [2]						
				N	Min.	Max.	HAFT [3]	Median (STMdR)	Mean (STMR)	Std. Dev.
Fruit	Monoamine salt (SC/L)	5 ppm (6.75-6.77)	0	2	0.259	0.738	0.738	0.714	0.714	0.393
Fruit	Dipotassium salt (SC/L)	3.5 ppm (4.80-4.81)	0	2	0.324	0.433	0.433	0.522	0.522	0.389

[1] The concentrations are expressed in acid equivalents, and the values in parentheses are the total application rate in terms of lb ae/A.
[2] Residues are expressed in terms of the free acid. The LOQ is 0.05 ppm.
[3] HAFT = Highest Average Field Trial.

D. CONCLUSION

The available field trial data are adequate and support the use of endothall-treated water for irrigation of cucumbers. The data support the use of the monoalkylamine salt of endothall in irrigation water at a concentration of 5 ppm ae and the use of the dipotassium salt of endothall in irrigation water at a concentration of 3.5 ppm ae. No more that six applications of treated water should be made per season with a minimum 7-day interval for application to the water. Results are for cucumbers at a 0-day PHI.

E. REFERENCES

None

F. DOCUMENT TRACKING

RDI: David Soderberg (5 June 2009); William Donovan (5 June 2009)
Petition Number: 8E7419
DP#: 356315
PC Code: 038901, 038904, and 038905

Template Version June 2005

Primary Evaluator	David Soderberg, Chemist, RABV, HED	Date: 5 June 2009
Approved by	William Donovan, Senior Scientist, RABV, HED	Date: 5 June 2009

This DER was originally prepared under contract by Dynamac Corporation (1910 Sedwick Road, Building 100, Suite B, Durham, NC 27713; submitted 3/30/2009). The DER has been reviewed by the Health Effects Division (HED) and revised as needed for clarity, correctness and to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORT:

47520705. Arsenovic, M. (2008) Endothall (Hydrothol 191): Magnitude of the Residue on Vegetable, Legume Group: Lab Project Number: Z9765. Z9765.07-ALS05 Unpublished study prepared by Interregional Research Project No. 4. 440 pages.

EXECUTIVE SUMMARY:

Interregional Research Project No. 4 (IR-4) submitted a soybean processing study reflecting the exposure of soybeans to endothall through the use of treated irrigation water. In a field trial conducted in IA (Zone 5) during 2007, a 2.0 lb ae/gal soluble concentrate (SC/L) formulation of endothall (monoalkylamine salt) was used to treat the irrigation water at a rate of 5 ppm ae. [In order to avoid the complications of different molecular weights for different salts, endothall concentrations are expressed as the free acid equivalents (ae).] The treated water was then applied using overhead sprinklers to soybeans as six broadcast foliar applications during seed and pod development at retreatment intervals (RTIs) of 6-8 days. A volume equivalent to 1 acre inch of water (~27,154 gal/A) was applied for each application. Based on the concentration of the endothall in the irrigation water and the amount of water applied, the application rate for endothall was equivalent to 1.13 lb ae/A/application, for a total of 6.77 lb ae/A/season.

Single bulk control and treated samples of soybeans were harvested at normal crop maturity, immediately following the last irrigation (0 days after treatment, DAT). The soybeans were processed into hulls, meal and refined oil using simulated commercial procedures. Samples were stored at ≤-10°C for up to 78 days (seeds) or 20 days (hulls, meal and oil) prior to analysis. The sample storage intervals and conditions are supported by the available storage stability data.

Residues of endothall (free acid) in/on soybean seed, hulls, meal and oil were determined using an adequate LC/MS/MS method (Method No. KP-242R1). For each commodity except oil, residues were extracted with water and then derivatized with heptafluoro-*p*-tolylhydrazine (HFTH) in 50% H_3PO_4. Oil samples were diluted with water and partitioned against hexane, and the aqueous soluble residues were then derivatized with HFTH. The derivatized residues from each matrix were then cleaned up by partitioning into methyl t-butyl ether (MTBE) followed by elution through an amine solid phase extraction (SPE) cartridge. Residues were then analyzed by LC/MS/MS using external standards for quantitation. The validated limit of quantitation (LOQ) for endothall is 0.05 ppm in each soybean matrix, and the estimated limit of detection (LOD) was reported to be 0.0001 ppm.

Following six overhead sprinkler applications of endothall (monoalkylamine salt) to soybeans at rates totaling 6.77 lb ae/A, endothall residues were 0.021 ppm in/on whole seeds, 0.083 ppm in/on hulls, 0.017 ppm in meal, and nondetectable (<0.0001 ppm) in refined oil. The processing factors were 3.9x for hulls, 0.8x for meal, and <0.005x for oil. The theoretical processing factors for soybean commodities are 11.3x for hulls, 2.2x for meal, and 12x for oil.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the soybean processing study is classified as scientifically acceptable. The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document, DP# 356315.

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported which would have an adverse impact on the validity of the study.

A. BACKGROUND INFORMATION

Endothall [7-oxabicyclo[2,2,1] heptane-2,3-dicarboxylic acid] is a selective contact herbicide, defoliant, desiccant, and aquatic algaecide that belongs to the dicarboxylic acid chemical class. The free acid of endothall (PC Code 038901) and its dipotassium (PC Code 038904) and alkylamine (PC Code 038905) salts are registered primarily as aquatic herbicides for the control a variety of plants in water bodies. This includes irrigation canals, but only with a 7 day holding period. They are also registered for desiccation/ defoliation of alfalfa/clover (grown for seed only), cotton, and potatoes prior to harvest, and for reduction of sucker branch growth in hops. Permanent tolerances are established for the combined residues of endothall and its monomethyl ester at 0.1 ppm in/on cotton seeds, fish, dried hops and potatoes, and at 0.05 ppm in/on rice grain and straw [40 CFR §180.293(a)(1)].

In conjunction with a petition for tolerances on a wide variety of irrigated crops (PP# 8E7419), IR-4 has submitted a soybean processing study reflecting irrigation of soybeans with endothall-treated water. The chemical structure and nomenclature of endothall and its monoalkylamine salt are listed in Table A.1. The physicochemical properties of technical grade endothall and its monoalkylamine salt are listed in Table A.2.

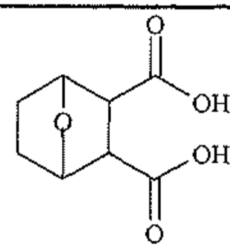
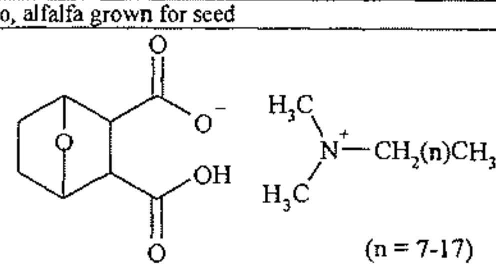
Table A.1. Endothall and Salts Nomenclature	
Chemical Structure	
Common name	Endothall
Molecular Formula	$C_8H_{10}O_5$
Molecular Weight	186.16
IUPAC name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid
CAS name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid
CAS #	145-73-3
PC Code	038901
Current Food/Feed Site Registration	Cotton, hops, potato, alfalfa grown for seed
Chemical Structure	 (n = 7-17)
Common name	Endothall, mono-N,N-dimethylalkyl amine salt
Molecular Formula	Not available
Molecular Weight	Average: 422
IUPAC name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid, compound with N,N-dimethylcocoamine
CAS name	Not available
CAS #	66330-88-9
PC Code	038905
Current Food/Feed Site Registration	Cotton, hops, potato, alfalfa grown for seed, aquatic uses

Table A.2. Physicochemical Properties of Endothall and Salts		
Parameter	Value	Reference
Endothall (acid)		
Melting point	108-110℃	D187593, D187590, and D187588, 5/5/93, K. Dockter
pH	2.7 at 25℃ (1% solution)	D187593, D187590, and D187588, 5/5/93, K. Dockter
Density, bulk density, or specific gravity	0.481 g/cm^3 (bulk) at 25℃	D187593, D187590, and D187588, 5/5/93, K. Dockter
Water solubility at 25℃	109.8 g/L 13.1 g/100 mL in water, pH 5 12.7 g/100 mL in water, pH 7 12.5 g/100 mL in water, pH 9	D166798, 7/2/92, K. Dockter D207011, 9/30/94, F. Toghrol
Solvent solubility at 25℃	3.4 g/100 mL in acetonitrile 2.4 g/100 mL in n-octanol 16.0 g/100 mL in tetrahydrofuran	D207011, 9/30/94, F. Toghrol
Vapor pressure	3.92 x 10^{-5} mm Hg at 24.3℃	D166798, 7/2/92, K. Dockter

Table A.2. Physicochemical Properties of Endothall and Salts		
Parameter	Value	Reference
Dissociation constant, pK_a	4.32 for Step 1 and 6.22 for Step 2 at 20℃ (0.2% solution in 20% basic ethanol); dissociation rate 1.8-2.3 x 10^3 µmho within 3-5 minutes at □25℃, by conductivity meter	D188708, 5/3/93, K. Dockter
Octanol/water partition coefficient	Not applicable to endothall acid	D166798, 7/2/92, K. Dockter
UV/visible absorption spectrum	Not available	
Endothall, mono-N,N-dimethylalkyl amine salt		
Boiling point	Not available	
pH	5.2 at 25℃ (1% solution)	D187593, D187590, and D187588, 5/5/93, K. Dockter
Density, bulk density, or specific gravity	1.028 g/mL at 25℃	D187593, D187590, and D187588, 5/5/93, K. Dockter
Water solubility at 25℃	≥49.2 g/100mL in water, pH 5 ≥51.6 g/100 mL in water, pH 7 ≥49.8 g/100 mL in water, pH 9	D210814, 8/9/95, S. Knizner
Solvent solubility at 25℃	≥102.5 g/100mL in acetonitrile ≥95.4 g/100 mL in n-octanol ≥104.3 g/100 mL in tetrahydrofuran	D210814, 8/9/95, S. Knizner
Vapor pressure	2.09 x 10^{-5} mm Hg at 25℃ (calculated; mixed mono- and dialkylamine (C8-C20))	D206344, 9/22/94, F. Toghrol
Dissociation constant, pK_a	4.24 for Step 1 and 6.07 for Step 2 at 20℃ for mixed mono- and dialkylamine (C8-C20) in acidified ethanol/water; dissociation complete □17 minutes (1.7 x 10^3 µmho) at 25℃	D198885, 4/7/94, F. Toghrol
Octanol/water partition coefficient	K_{OW} 2.097 at concentrations of 8.9 x 10^{-3} M and 8.9 x 10^{-4} M, at 25℃	D209995, 1/20/95, L. Edwards
UV/visible absorption spectrum	Not available	

B. EXPERIMENTAL DESIGN

B.1. Application and Crop Information

In a field trial conducted in IA (Zone 5) during 2007, soybeans were irrigated with endothall-treated water using overhead sprinklers (Table B.1.1). The irrigation water was treated with endothall (2.0 lb ae/gal SC/L monoalkylamine salt) at a concentration of ~5 ppm, acid equivalent. The treated field was irrigated six times during seed and pod development at RTIs of 6-8 days. A volume equivalent to ~1 acre inch of water (27,154 gal/A) was applied for each irrigation. Based on the concentration of the endothall and the amount of water applied, application rate for endothall was equivalent to 1.13 lb ae/A/application, for a total of 6.77 lb ae/A/season.

TABLE B.1.1. Study Use Pattern.							
Location (City, State; Year) Trial ID	End-Use Product	Application Information					
		Method; Timing	Concen. [1]	Volume (gal/A) [2]	Single Rate (lb ae/A) [3]	RTI [3] (days)	Total Rate (lb ae/A) [3]
Richland, IA 2007 IAS15	2.0 lb/gal SC	Six broadcast foliar application from flowering through fruit maturation using overhead sprinklers.	5.00	27,154	1.13	6-8	6.77

[1] The concentrate of endothall (in acid equivalents) in the irrigation water. No adjuvants were included in the irrigation water.
[2] The target irrigation rate was 1 acre inch of water or 27,154 gal/A.
[3] The equivalent field use rates were calculated by the reviewer based on the concentration of the endothall (ae), the application volume and plot size.
[4] RTI = Retreatment Interval.

B.2. Sample Handling and Processing Procedures

Single control and treated bulk samples of soybean seeds (≥73 lb/sample) were harvested at 0 DAT, and shipped by ACDS Freezer truck to the processing facility, GLP Technologies, Navasota, TX. Samples were placed in frozen storage ≤10°F prior to processing, which was completed within 42-44 days of harvest. Samples were processed into hulls, meal and refined oil using simulated commercial procedures (Figure B.1).

Seeds were first dried to a moisture content of ≤13.5%. Light impurities and foreign particles were then separated and the clean, whole seed was fed into a roller mill to crack the hull and liberate the kernel. After hulling, hulls and kernels were separated. The kernel material was heated to 160-175°F and flaked, which were extruded into collets. The collets were extracted with hexane repeatedly and extracted collets were desolventized in a paddle blender to remove residual solvent. Crude oil and hexane was passed through a laboratory vacuum evaporator to separate the crude oil and hexane. The crude oil was alkali refined to separate the soapstock from the oil.

Samples were transferred to frozen storage (≤-12°C) immediately after processing and shipped frozen by overnight courier on dry ice 3 days after processing to the analytical laboratory, ALS Laboratory Group (Edmonton, AB, Canada). At ALS, the processed samples were stored frozen (≤-10°C) prior to analysis.

C. RESULTS AND DISCUSSION

The LC/MS/MS method used for determining residues of endothall in/on soybeans and soybean processed fractions was adequately validated prior to and in conjunction with the analysis of field trial samples. Average method validation recoveries (±SD) were 97 ± 16% for soybean seeds and 101 ± 8% for soybean oil (Table C.1). Concurrent recoveries averaged 86 ± 9% for soybeans and 84% for soybean refined oil (n=2). Apparent residues of endothall were <LOQ in/on control samples. Adequate sample calculations and example chromatograms were provided and the fortification levels used for method recoveries were similar in magnitude to the measured residue levels.

Soybean seeds and processed products were stored frozen at ≤-10°C for up to 78 and 20 days, respectively, prior to analysis (Table C.2). Adequate storage stability data are available indicating that endothall is stable in frozen soybean seeds and oil for up to 305-316 days (47520719.der, under review). These data will support the storage durations and conditions for the soybean processing study.

Following six overhead sprinkler applications of endothall (monoalkylamine salt) to soybeans at rates totaling 6.77 lb ae/A, residues were 0.021 ppm in/on whole seeds (<LOQ), 0.083 ppm in/on hulls, 0.017 ppm in meal, and nondetectable (<0.0001 ppm) in refined oil (Table C.3). Although residues were <LOQ, detectable residues of endothall were found in seeds and meal. Therefore, values <LOQ, but ≥LOD were used for calculating the processing factors. The processing factors were 3.9x for hulls, 0.8x for meal, and <0.005x for oil. The theoretical processing factors for soybean commodities are 11.3x for hulls, 2.2x for meal, and 12x for oil.

TABLE C.1. Summary of Method Validation and Concurrent Recoveries of Endothall from Soybeans.

Matrix	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean ± Std. Dev. (%)
Method Validation				
Soybean seed	0.05	3	83, 76, 71	76 ± 6
	0.5	3	108, 101, 115	108 ±7
	5.0	3	104, 104, 113	107 ±5
	Total	9	**71-115**	**97 ± 16**
Soybean, refined oil	0.05	3	86, 100, 97	94 ± 7
	0.5	3	111, 104, 114	110 ± 5
	5.0	3	99, 98, 100	99 ± 1
	Total	9	**86-114**	**101 ± 8**
Concurrent Recoveries				
Soybean seed (dried)	0.05	3	92, 99, 91	94 ± 4
	0.5	3	81, 75, 78	78 ± 3
	Total	6	75-99	86 ± 9
Soybean, refined oil	0.05	1	92	84
	0.5	1	76	

Standard deviations are calculated for data sets having ≥3 values.

TABLE C.2. Summary of Storage Conditions.

Matrix	Storage Temperature (°C)	Actual Storage Duration (days)[1]	Interval of Demonstrated Storage Stability (days)[2]
Whole seed	≤-10	78	305-316
Meal		17	
Hulls		19	
Refined oil		20	

[1] Interval from harvest to extraction for analysis. Extracts were stored up to 9 days prior to analysis.
[2] Endothall is stable in frozen soybean seeds and oil for up to 305-316 days (47520719.der under review).

TABLE C.3. Residue Data from Soybean Processing Study with Endothall Monoalkylamine Salt (SC/L).

RAC	Processed Commodity	Total Rate		PHI (days)	Residues (ppm)[2]	Processing Factor[3]
		ppm	lb ae/A			
Soybean	Whole Seed (RAC)	5.0	6.77	0	(0.0212)	--
	Hulls				0.0829	3.9x
	Meal				(0.0165)	0.78x
	Refined oil				ND	<0.005x

[1] The rate is expressed both in terms of the concentration in the irrigation water (ppm) and the total amount (lb ae/A) applied.
[2] Expressed in acid equivalents. The LOQ is 0.05 ppm and the LOD estimated to be 0.0001 ppm. Values <LOQ but ≥LOD are listed in parentheses.
[3] Values <LOQ but ≥LOD were used for calculating processing factors.'
ND = not detected.

D. CONCLUSION

The soybean processing study is adequate. Endothall residues were reduced in both soybean meal (0.8x) and oil (<0.005x), but concentrated in soybean hulls (3.9x).

E. REFERENCES

None

F. DOCUMENT TRACKING

RDI: David Soderberg (5 June 2009); William Donovan (5 June 2009)
Petition Number: 8E7419
DP#: 356315
PC Code: 038901 and 038905

Template Version June 2005

Primary Evaluator	David Soderberg, Chemist, RABV, HED	Date: 5 June 2009
Approved by	William H. Donovan William Donovan, Senior Scientist, RABV, HED	Date: 5 June 2009

This DER was originally prepared under contract by Dynamac Corporation (1910 Sedwick Road, Building 100, Suite B, Durham, NC 27713; submitted 3/27/2009). The DER has been reviewed by the Health Effects Division (HED) and revised as needed for clarity, correctness and to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORT:

47520708. Arsenovic, M. (2008) Endothall (Hydrothol 191): Magnitude of the Residue on Fruit, Citrus Group: Lab Project Number: Z9759, Z9759.07-CER08 Unpublished study prepared by Interregional Research Project No. 4. 230 pages.

EXECUTIVE SUMMARY:

Interregional Research Project No. 4 (IR-4) submitted a citrus processing study reflecting the exposure of orange trees to endothall through the use of treated irrigation water. In a field trial conducted in FL (Zone 3) during 2006, a 2.0 lb ae/gal soluble concentrate (SC/L) formulation of endothall (monoalkylamine salt) was used to treat the irrigation water at a rate of 5 ppm ae. [In order to avoid the complications of different molecular weights for different salts, endothall concentrations are expressed as the free acid equivalents (ae).] The treated water was then applied using overhead sprinklers to the orange trees as six broadcast foliar applications during fruit development at retreatment intervals (RTIs) of 5-6 days. A volume equivalent to 1 acre inch of water (~27,154 gal/A) was applied for each application. Based on the concentration of the endothall and the amount of water applied, the application rate for endothall was equivalent to 1.10 lb ae/A/application, for a total of 6.63 lb ae/A/season.

Single bulk control and treated samples of oranges were harvested at normal crop maturity, immediately following the last irrigation (0 days after treatment, DAT). The fruit was processed into juice, oil and dried pulp using simulated commercial procedures. Samples of whole fruit, juice, oil, and dried pulp were stored at ≤-18°C for up to 121 days prior to analysis. The sample storage intervals and conditions are supported by the available storage stability data.

Residues of endothall (free acid) in/on whole fruits and each processed fraction were determined using an adequate LC/MS/MS method (Method No. KP-242R1). Residues in whole fruits and pulp samples were extracted with water and then derivatized with heptafluoro-*p*-tolylhydrazine (HFTH) in 50% H_3PO_4. Juice samples were first diluted with water and then derivatized wit HFTH. Oil samples were diluted with water and partitioned against hexane, and the aqueous soluble residues were then derivatized with HFTH. The derivatized residues from each matrix were cleaned up by partitioning into methyl t-butyl ether (MTBE) followed by elution through an amine solid phase extraction (SPE) cartridge. Residues were then analyzed by LC/MS/MS using external standards for quantitation. The validated limit of quantitation (LOQ) for endothall is 0.05 ppm in each citrus matrix, and the estimated limit of detection (LOD) was 0.0025 ppm.

Although endothall residues were <LOQ in/on whole orange fruits and in each processed fraction, residues above the LOD were detected in each fraction except oil. Residues were detected at 0.019 ppm in/on whole fruit and at 0.014 ppm in juice, 0.041 ppm in dried pulp. Residues in oil were <LOD. Based on these residue values the processing factors were 0.7x for juice, 2.2x for dried pulp, and <0.2x for oil. The theoretical processing factors for citrus juice and oil are 2x and 1000x, respectively.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the citrus processing study is classified as scientifically acceptable. The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document, DP# 356315.

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported which would have an adverse impact on the validity of the study.

A. BACKGROUND INFORMATION

Endothall [7-oxabicyclo[2,2,1] heptane-2,3-dicarboxylic acid] is a selective contact herbicide, defoliant, desiccant, and aquatic algaecide that belongs to the dicarboxylic acid chemical class. The free acid of endothall (PC Code 038901) and its dipotassium (PC Code 038904) and alkylamine (PC Code 038905) salts are registered primarily as aquatic herbicides for the control a variety of plants in water bodies. This includes irrigation canals, but only with a 7 day holding period. They are also registered for desiccation/ defoliation of alfalfa/clover (grown for seed only), cotton, and potatoes prior to harvest, and for reduction of sucker branch growth in hops. Permanent tolerances are established for the combined residues of endothall and its monomethyl ester at 0.1 ppm in/on cotton seeds, fish, dried hops and potatoes, and at 0.05 ppm in/on rice grain and straw [40 CFR §180.293(a)(1)].

In conjunction with a petition for tolerances on a wide variety of irrigated crops (PP# 8E7419), IR-4 has submitted a citrus processing study reflecting irrigation of orange trees with endothall-treated water. The chemical structure and nomenclature of endothall and its monoalkylamine salt are listed in Table A.1. The physicochemical properties of technical grade endothall and its monoalkylamine salt are listed in Table A.2.

Table A.1. Nomenclature of Endothall and its Monoalkylamine Salt.

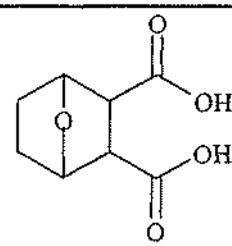
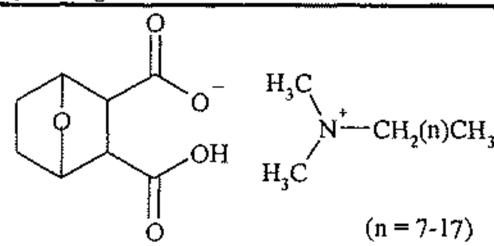
Table A.1. Nomenclature of Endothall and its Monoalkylamine Salt.	
Chemical Structure	
Common name	Endothall
Molecular Formula	$C_8H_{10}O_5$
Molecular Weight	186.16
IUPAC name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid
CAS name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid
CAS #	145-73-3
PC Code	038901
Current Food/Feed Site Registration	Cotton, hops, potato, alfalfa grown for seed
Chemical Structure	 (n = 7-17)
Common name	Endothall, mono-N,N-dimethylalkyl amine salt
Molecular Formula	Not available
Molecular Weight	Average: 422
IUPAC name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid, compound with N,N-dimethylcocoamine
CAS name	Not available
CAS #	66330-88-9
PC Code	038905
Current Food/Feed Site Registration	Cotton, hops, potato, alfalfa grown for seed, aquatic uses

Table A.2. Physicochemical Properties of Endothall and Its Monoalkylamine Salt.		
Parameter	Value	Reference
Endothall (acid)		
Melting point	108-110℃	D187593, D187590, and D187588, 5/5/93, K. Dockter
pH	2.7 at 25℃ (1% solution)	D187593, D187590, and D187588, 5/5/93, K. Dockter
Density, bulk density, or specific gravity	0.481 g/cm^3 (bulk) at 25℃	D187593, D187590, and D187588, 5/5/93, K. Dockter
Water solubility at 25℃	109.8 g/L 13.1 g/100 mL in water, pH 5 12.7 g/100 mL in water, pH 7 12.5 g/100 mL in water, pH 9	D166798, 7/2/92, K. Dockter D207011, 9/30/94, F. Toghrol
Solvent solubility at 25℃	3.4 g/100 mL in acetonitrile 2.4 g/100 mL in n-octanol 16.0 g/100 mL in tetrahydrofuran	D207011, 9/30/94, F. Toghrol
Vapor pressure	3.92 x 10^{-5} mm Hg at 24.3℃	D166798, 7/2/92, K. Dockter
Dissociation constant, pK_a	4.32 for Step 1 and 6.22 for Step 2 at 20℃ (0.2% solution in 20% basic ethanol); dissociation rate 1.8-2.3 x 10^1 μmho within 3-5 minutes at □25℃, by conductivity meter	D188708, 5/3/93, K. Dockter
Octanol/water partition coefficient	Not applicable to endothall acid	D166798, 7/2/92, K. Dockter
UV/visible absorption spectrum	Not available	
Endothall, mono-N,N-dimethylalkyl amine salt		
Boiling point	Not available	
pH	5.2 at 25℃ (1% solution)	D187593, D187590, and D187588, 5/5/93, K. Dockter
Density, bulk density, or specific gravity	1.028 g/mL at 25℃	D187593, D187590, and D187588, 5/5/93, K. Dockter
Water solubility at 25℃	≥49.2 g/100mL in water, pH 5 ≥51.6 g/100 mL in water, pH 7 ≥49.8 g/100 mL in water, pH 9	D210814, 8/9/95, S. Knizner
Solvent solubility at 25℃	≥102.5 g/100mL in acetonitrile ≥95.4 g/100 mL in n-octanol ≥104.3 g/100 mL in tetrahydrofuran	D210814, 8/9/95, S. Knizner
Vapor pressure	2.09 x 10^{-5} mm Hg at 25℃ (calculated; mixed mono- and dialkylamine (C8-C20))	D206344, 9/22/94, F. Toghrol
Dissociation constant, pK_a	4.24 for Step 1 and 6.07 for Step 2 at 20℃ for mixed mono- and dialkylamine (C8-C20) in acidified ethanol/water; dissociation complete □17 minutes (1.7 x 10^3 μmho) at 25℃	D198885, 4/7/94, F. Toghrol
Octanol/water partition coefficient	K_{OW} 2.097 at concentrations of 8.9 x 10^{-3} M and 8.9 x 10^{-4} M, at 25℃	D209995, 1/20/95, L. Edwards
UV/visible absorption spectrum	Not available	

B. EXPERIMENTAL DESIGN

B.1. Application and Crop Information

In a field trial conducted in FL during 2006, orange trees were irrigated with endothall-treated water using overhead sprinklers (Table B.1.1). The irrigation water was treated with endothall (2.0 lb ae/gal SC/L monoalkylamine salt) at a concentration of ~5 ppm, acid equivalent. The trees were irrigated six times during fruit development at RTIs of 5-6 days. A volume equivalent to ~1 acre inch of water (27,154 gal/A) was applied for each irrigation. Based on the

concentration of the endothall and the amount of water applied, application rate for endothall was equivalent to 1.10 lb ae/A/application, for a total of 6.63 lb ae/A/season.

TABLE B.1.1. Study Use Pattern.

Location (City, State; Year) Trial ID	End-Use Product	Application Information					
		Method; Timing	Concen. [1]	Volume (gal/A) [2]	Single Rate (lb ae/A) [3]	RTI [4] (days)	Total Rate (lb ae/A) [3]
Oviedo, FL 2006 FL$10	2.0 lb/gal SC	Six broadcast foliar application during fruit development using overhead sprinklers.	5.0	26,701-26,721	1.10	5-6	6.63

1 The concentrate of endothall (in acid equivalents) in the irrigation water. No adjuvants were included in the irrigation water.
2 The target irrigation rate was 1 acre inch of water or 27,154 gal/A.
3 The equivalent field use rates were calculated by the reviewer based on the concentration of the endothall (ae), the application volume and plot size.
4 RTI = Retreatment Interval.

B.2. Sample Handling and Processing Procedures

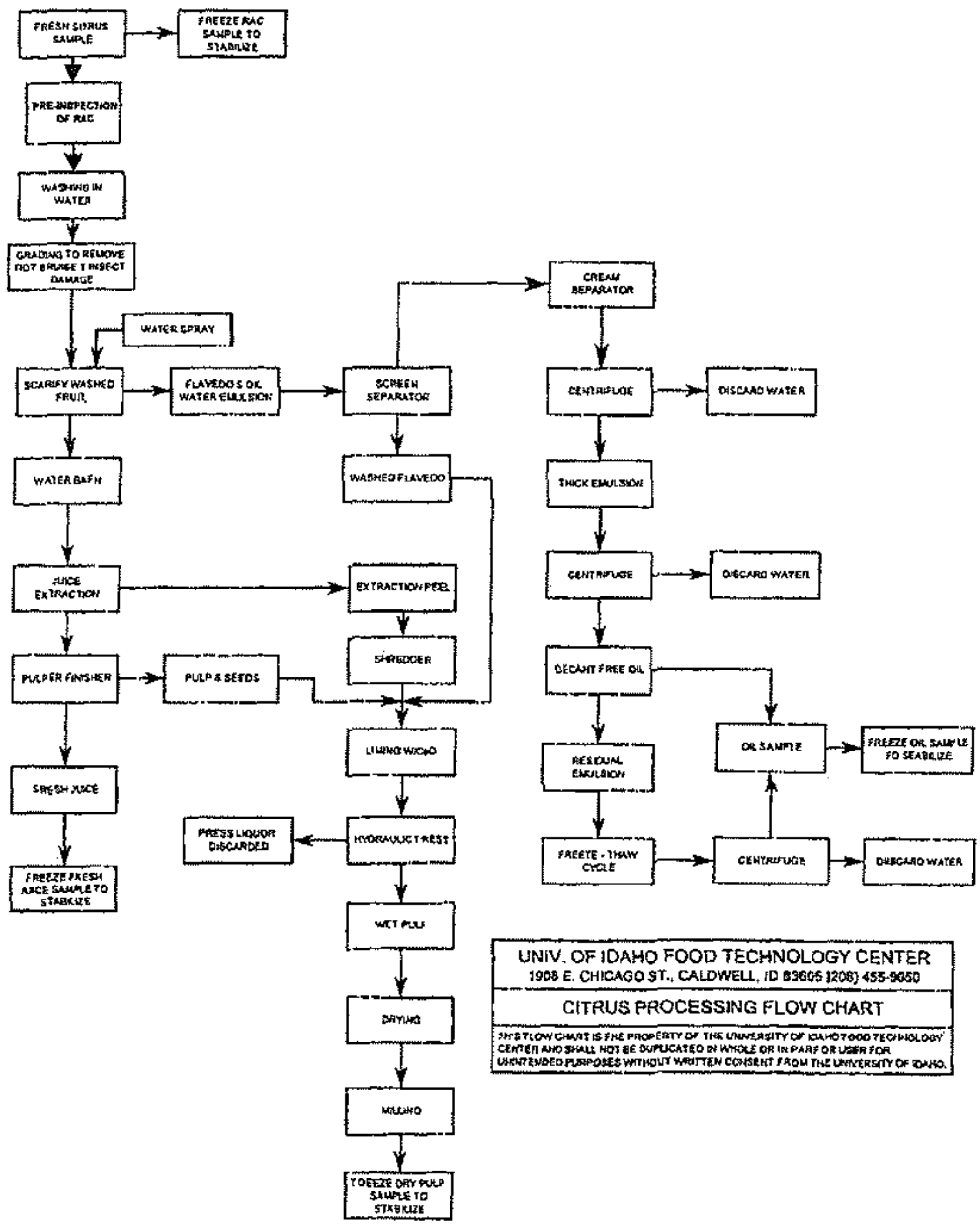
Single control and treated samples of oranges (~500 lb/sample) were harvested at 0 DAT (after the sixth application) and were shipped fresh under ambient conditions on the day of harvest via overnight courier to the processing facility, Englar Food Laboratories, Inc., Caldwell, ID. Samples were received by the processor two days after harvest and were placed in cool storage 4±3°C prior to processing, which was completed within 5-9 days of harvest.

Oranges were processed into dried pulp, oil and juice according to simulated commercial procedures (Figure B.1). The oranges were washed for 5 minutes in water, and abraded to collect the oil. The oranges were then extracted using a commercial juice extractor to produce the juice fraction. For dried pulp, the peel was shredded, combined with the waste from the oil extraction and seeds to generate wet peel. Lime was added and the wet pulp was dried to 4.4-4.5% moisture on an air dryer.

Samples of whole fruit and each processed fraction were placed in frozen storage (-17 ± 8°C) immediately after processing and shipped 20-24 days later by overnight courier on dry ice to the analytical laboratory, Cerexagri, Inc. (King of Prussia, PA). At Cerexagri, the processed samples were stored at ≤-18°C until analysis.

FIGURE B.1. **Processing Flowchart for Oranges.**

CITRUS PROCESSING
PILOT PLANT LABORATORY



B.3. Analytical Methodology

Residues of the free acid of endothall in/on citrus fruits and processed citrus fruit fractions were determined using a LC/MS/MS method (Method No. KP-242R1) entitled "Analytical Method for Determination of Endothall in Crops", issued 5/4/2007.

For this method, residues in whole fruit and pulp were extracted twice by homogenization with water followed by centrifugation and filtering. For juice, the sample was only diluted with water prior to derivatization. For oil, the sample was mixed with water and then partitioned 3x with hexane, discarding the hexane phases. Residue in the resulting water fractions from each matrix were then derivatized with HFTH in 50% H_3PO_4 at 100-120°C for 90 minutes. After cooling, the derivatized residues were partitioned into MTBE, evaporated to dryness, and reconstituted in hexane:MTBE (1:1 v:v). Residues were then cleaned using an amine SPE cartridge eluted with methanol:MTBE (1:4). Residues were analyzed by LC/MS/MS using external standards. The m/z 397→166 ion transition was used for quantifying residues, and residues are expressed in acid equivalents. The validated LOQ for endothall is 0.05 ppm, and the estimated LOD is 0.0025 ppm.

For method validation, control samples of whole fruits were fortified with endothall at 0.05-5.0 ppm. For concurrent recoveries, control sample were fortified with endothall at 0.05-1.0 ppm for whole fruit and at 0.05 and 0.50 ppm for each processed fraction.

C. RESULTS AND DISCUSSION

The LC/MS/MS method used for determining residues of endothall in/on oranges and orange processed products was adequately validated prior to and in conjunction with the analysis of field trial samples. For whole fruits, the method validation recoveries averaged 75% with a standard deviation of 4%, and the concurrent recoveries averaged 73% with a standard deviation of 2% (Table C.1). The average concurrent recovery was 77% for dried pulp, 90% for juice and 91% for oil. Apparent residues of endothall were <LOD in/on control samples of each matrix. Adequate sample calculations and example chromatograms were provided and the fortification levels used for method recoveries were similar in magnitude to the measured residue levels.

Orange fruit, dried pulp, juice and oil samples were stored frozen at ≤-18°C for up to 121 days prior to analysis (Table C.2). Adequate storage stability data are available indicating that endothall is stable under frozen storage conditions for up to 467 days in tomatoes (acid fruit) and for up to 306 days in soybean oil (47520719.der, under review). These stability data will support the storage durations and conditions for the orange processing study.

Endothall residues were <0.05 ppm in/on whole fruits and each processed fraction (Table C.3). Although residues were <LOQ, residues above the LOD were detected in each fraction except oil. Endothall residues were detected at 0.019 ppm in/on whole fruit used for processing and at 0.014 ppm in juice, 0.041 ppm in dried pulp. Residues in oil were <LOD. Based on these residue values the processing factors were 0.7x for juice, 2.2x for dried pulp, and <0.2x for oil. The theoretical processing factors for citrus juice and oil are 2x and 1000x, respectively.

TABLE C.1. Summary of Method Validation and Concurrent Recoveries of Endothall from Oranges and Orange Processed Fractions.				
Matrix	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean ± Std. Dev. (%)
Method Validation				
Fruit	0.05	3	76, 72, 74	74 ± 2
	0.5	3	72, 72, 73	72 ± 1
	5.0	3	76, 73, 85	78 ± 6
	Total	**9**	**72-85**	**75 ± 4**
Concurrent Recoveries				
Fruit	0.05	2	76, 71	74
	0.5	1	74	74
	1.0	1	72	72
	Total	**4**	**71-76**	**73 ± 2**
Dried pulp	0.05	1	83	77
	0.5	1	71	
Juice	0.05	1	75	90
	0.5	1	104	
Oil	0.05	1	95	91
	0.5	1	87	

[1] Standard deviations are calculated for data sets having ≥3 values.

TABLE C.2. Summary of Storage Conditions.			
Matrix	Storage Temperature (°C)	Actual Storage Duration (days)	Interval of Demonstrated Storage Stability (days) [2]
Orange, unwashed fruit (RAC)	≤-18	109	467
Dried pulp		121	
Juice		114	
Oil		120	306

[1] Interval from harvest to extraction for analysis. Extracts were stored up to 2 days prior to analysis.
[2] Endothall is stable in frozen tomatoes for up to 467 days and frozen soybean oil for up to 306 days (47520719.der under review).

TABLE C.3. Residue Data from Orange Processing Study with Endothall.						
RAC	Processed Commodity	Total Rate [1]		PHI (days)	Residues (ppm) [1]	Processing Factor
		ppm	lb ae/A			
Orange Fruit	Whole unwashed fruit (RAC)	5.0	6.63	0	0.019	--
	Dried pulp				0.041	2.2x
	Juice				0.014	0.7x
	Oil				ND	<0.2x

[1] The rate is expressed both in terms of the concentration in the irrigation water (ppm) and the total amount (lb ae/A) applied.
[2] Expressed in acid equivalents. The LOQ is 0.05 ppm and the LOD estimated to be 0.0025 ppm. Values <LOQ but ≥LOD are listed in parentheses.
[3] Values <LOQ but ≥LOD were used for calculating processing factors

D. CONCLUSION

The orange processing study is adequate. Endothall residues were reduced in both citrus juice (0.7x) and oil (<0.2x), but concentrated in dried pulp (2.2x).

E. REFERENCES

None

F. DOCUMENT TRACKING

RDI: David Soderberg (5 June 2009); William Donovan (5 June 2009)
Petition Number: 8E7419
DP#: 356315
PC Codes: 038901 and 038905

Template Version June 2005

Primary Evaluator	David Soderberg, Chemist, RABV, HED	Date; 5 June 2009
Approved by	William Donovan, Senior Scientist, RABV, HED	Date: 5 June 2009

This DER was originally prepared under contract by Dynamac Corporation (1910 Sedwick Road, Building 100, Suite B, Durham, NC 27713; submitted 3/27/2009). The DER has been reviewed by the Health Effects Division (HED) and revised as needed for clarity, correctness and to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORT:

47520709. Arsenovic, M. (2008) Endothall (Hydrothol 191): Magnitude of the Residue on Fruit, Pome Group: Lab Project Number: Z9767, Z9767.07-CER05 Unpublished study prepared by Interregional Research Project No. 4. 255 pages.

EXECUTIVE SUMMARY:

Interregional Research Project No. 4 (IR-4) submitted an apple processing study reflecting the exposure of apple trees to endothall through the use of treated irrigation water. In a field trial conducted in NY (Zone 1) during 2006, a 2.0 lb ae/gal soluble concentrate (SC/L) formulation of endothall (monoalkylamine salt) was used to treat the irrigation water at a rate of 5 ppm ae. [In order to avoid the complications of different molecular weights for different salts, endothall concentrations are expressed as the free acid equivalents (ae).] The treated water was then applied using overhead sprinklers to the apple trees as six broadcast foliar applications during fruit development at 7-day retreatment intervals (RTIs). A volume equivalent to 1 acre inch of water (~27,154 gal/A) was applied for each application. Based on the concentration of the endothall and the amount of water applied, the application rate for endothall was equivalent to 1.13 lb ae/A/application, for a total of 6.79 lb ae/A/season.

Single bulk control and treated samples of apples were harvested at normal crop maturity, immediately following the last irrigation (0 days after treatment, DAT). The fruit was processed into juice and wet pomace using simulated commercial procedures. Samples of whole fruit, juice and wet pomace were stored at ≤-18°C for up to 286 days prior to analysis. The sample storage intervals and conditions are supported by the available storage stability data.

Residues of endothall (free acid) in/on apple fruit, juice and wet pomace were determined using an adequate LC/MS/MS method (Method No. KP-242R1). Residues were extracted with water and then derivatized with heptafluoro-*p*-tolylhydrazine (HFTH) in 50% H_3PO_4. The derivatized residues from each matrix were cleaned up by partitioning into methyl t-butyl ether (MTBE) and elution through an amine solid phase extraction (SPE) cartridge. Residues were then analyzed by LC/MS/MS using external standards for quantitation. The validated limit of quantitation

(LOQ) for endothall is 0.05 ppm in each apple matrix, and the estimate limit of detection (LOD) was 0.0025 ppm.

Residues of endothall averaged 0.033 ppm in/on whole fruit (<LOQ) and were 0.041 ppm in juice and 0.091 ppm in wet pomace. The calculated processing factors were 1.2x for juice and 2.8x for wet pomace.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the apple processing study is classified as scientifically acceptable. The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document, DP# 356315.

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported which would have an adverse impact on the validity of the study.

A. BACKGROUND INFORMATION

Endothall [7-oxabicyclo[2,2,1] heptane-2,3-dicarboxylic acid] is a selective contact herbicide, defoliant, desiccant, and aquatic algicide that belongs to the dicarboxylic acid chemical class. The free acid of endothall (PC Code 038901) and its dipotassium (PC Code 038904) and alkylamine (PC Code 038905) salts are registered primarily as aquatic herbicides for the control a variety of plants in water bodies. This includes irrigation canals, but only with a 7 day holding period. They are also registered for desiccation/ defoliation of alfalfa/clover (grown for seed only), cotton, and potatoes prior to harvest, and for reduction of sucker branch growth in hops. Permanent tolerances are established for the combined residues of endothall and its monomethyl ester at 0.1 ppm in/on cotton seeds, fish, dried hops and potatoes, and at 0.05 ppm in/on rice grain and straw [40 CFR §180.293(a)(1)].

In conjunction with a petition for tolerances on a wide variety of irrigated crops (PP# 8E7419), IR-4 has submitted a apple processing study reflecting irrigation of apple trees with endothall-treated water. The chemical structure and nomenclature of endothall and its monoalkylamine salt are listed in Table A.1. The physicochemical properties of technical grade endothall and its monoalkylamine salt are listed in Table A.2.

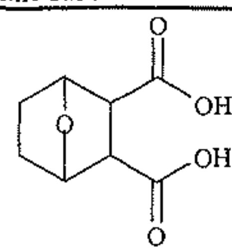
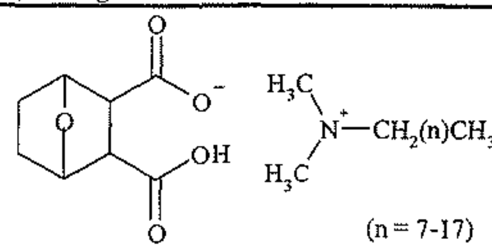
Table A.1. Nomenclature of Endothall and its Monoalkylamine Salt.	
Chemical Structure	
Common name	Endothall
Molecular Formula	$C_8H_{10}O_5$
Molecular Weight	186.16
IUPAC name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid
CAS name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid
CAS #	145-73-3
PC Code	038901
Current Food/Feed Site Registration	Cotton, hops, potato, alfalfa grown for seed
Chemical Structure	 (n = 7-17)
Common name	Endothall, mono-N,N-dimethylalkyl amine salt
Molecular Formula	Not available
Molecular Weight	Average: 422
IUPAC name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid, compound with N,N-dimethylcocoamine
CAS name	Not available
CAS #	66330-88-9
PC Code	038905
Current Food/Feed Site Registration	Cotton, hops, potato, alfalfa grown for seed, aquatic uses

Table A.2. Physicochemical Properties of Endothall and Its Monoalkylamine Salt.		
Parameter	Value	Reference
Endothall (acid)		
Melting point	108-110℃	D187593, D187590, and D187588, 5/5/93, K. Dockter
pH	2.7 at 25℃ (1% solution)	D187593, D187590, and D187588, 5/5/93, K. Dockter
Density, bulk density, or specific gravity	0.481 g/cm^3 (bulk) at 25℃	D187593, D187590, and D187588, 5/5/93, K. Dockter
Water solubility at 25℃	109.8 g/L 13.1 g/100 mL in water, pH 5 12.7 g/100 mL in water, pH 7 12.5 g/100 mL in water, pH 9	D166798, 7/2/92, K. Dockter D207011, 9/30/94, F. Toghrol
Solvent solubility at 25℃	3.4 g/100 mL in acetonitrile 2.4 g/100 mL in n-octanol 16.0 g/100 mL in tetrahydrofuran	D207011, 9/30/94, F. Toghrol
Vapor pressure	3.92 x 10^{-5} mm Hg at 24.3℃	D166798, 7/2/92, K. Dockter
Dissociation constant, pK_a	4.32 for Step 1 and 6.22 for Step 2 at 20℃ (0.2% solution in 20% basic ethanol); dissociation rate 1.8-2.3 x 10^3 μmho within 3-5 minutes at □25℃, by conductivity meter	D188708, 5/3/93, K. Dockter
Octanol/water partition coefficient	Not applicable to endothall acid	D166798, 7/2/92, K. Dockter
UV/visible absorption spectrum	Not available	
Endothall, mono-N,N-dimethylalkyl amine salt		
Boiling point	Not available	
pH	5.2 at 25℃ (1% solution)	D187593, D187590, and D187588, 5/5/93, K. Dockter
Density, bulk density, or specific gravity	1.028 g/mL at 25℃	D187593, D187590, and D187588, 5/5/93, K. Dockter
Water solubility at 25℃	≥49.2 g/100mL in water, pH 5 ≥51.6 g/100 mL in water, pH 7 ≥49.8 g/100 mL in water, pH 9	D210814, 8/9/95, S. Knizner
Solvent solubility at 25℃	≥102.5 g/100mL in acetonitrile ≥95.4 g/100 mL in n-octanol ≥104.3 g/100 mL in tetrahydrofuran	D210814, 8/9/95, S. Knizner
Vapor pressure	2.09 x 10^{-5} mm Hg at 25℃ (calculated; mixed mono- and dialkylamine (C8-C20))	D206344, 9/22/94, F. Toghrol
Dissociation constant, pK_a	4.24 for Step 1 and 6.07 for Step 2 at 20℃ for mixed mono- and dialkylamine (C8-C20) in acidified ethanol/water; dissociation complete □17 minutes (1.7 x 10^3 μmho) at 25℃	D198885, 4/7/94, F. Toghrol
Octanol/water partition coefficient	K_{OW} 2.097 at concentrations of 8.9 x 10^{-3} M and 8.9 x 10^{-4} M, at 25℃	D209995, 1/20/95, L. Edwards
UV/visible absorption spectrum	Not available	

B. EXPERIMENTAL DESIGN

B.1. Application and Crop Information

In a field trial conducted in NY during 2006, apple trees were irrigated with endothall-treated water using overhead sprinklers (Table B.1.1). The irrigation water was treated with endothall (2.0 lb ae/gal SC/L monoalkylamine salt) at a concentration of ~5 ppm, acid equivalent. The trees were irrigated six times during fruit development at RTIs of 7 days. A volume equivalent to ~1 acre inch of water (27,154 gal/A) was applied for each irrigation. Based on the

concentration of the endothall and the amount of water applied, application rate for endothall was equivalent to 1.13 lb ae/A/application, for a total of 6.79 lb ae/A/season.

TABLE B.1.1. Study Use Pattern.

Location (City, State; Year) Trial ID	End-Use Product	Application Information					
		Method; Timing	Concen. (ppm) [1]	Volume (gal/A) [2]	Single Rate (lb ae/A) [3]	RTI [4] (days)	Total Rate (lb ae/A) [3]
North Rose, NY 2006 NY$29	2.0 lb ae/gal SC/L	Six broadcast foliar application during fruit development using overhead sprinklers.	5.01	27,089	1.13	7	6.79

[1] The concentrate of endothall (in acid equivalents) in the irrigation water. No adjuvants were included in the irrigation water.
[2] The target irrigation rate was 1 acre inch of water or 27,154 gal/A.
[3] The equivalent field use rates were calculated by the reviewer based on the concentration of the endothall (ae), the application volume and plot size.
[4] RTI = Retreatment Interval.

B.2. Sample Handling and Processing Procedures

Single bulk control and treated samples (53-63 lbs/sample) of apple fruit were harvested at 0 DAT. The samples were shipped fresh on the day of harvest to the processing facility, ACDS Research, Inc. (North Rose, NY), where samples were stored in a cooler until processing. The fruit samples were processed on the day of harvest into juice and wet pomace using simulated commercial procedures (Figure B.1). After processing, the whole fruit, juice, and wet pomace samples were immediately stored at ≤-15°C. The samples were shipped 23 days later by freezer truck to the analytical laboratory, Cerexagi, Inc. (King of Prussia, PA), where the samples were processed and stored at -18°C until analysis.

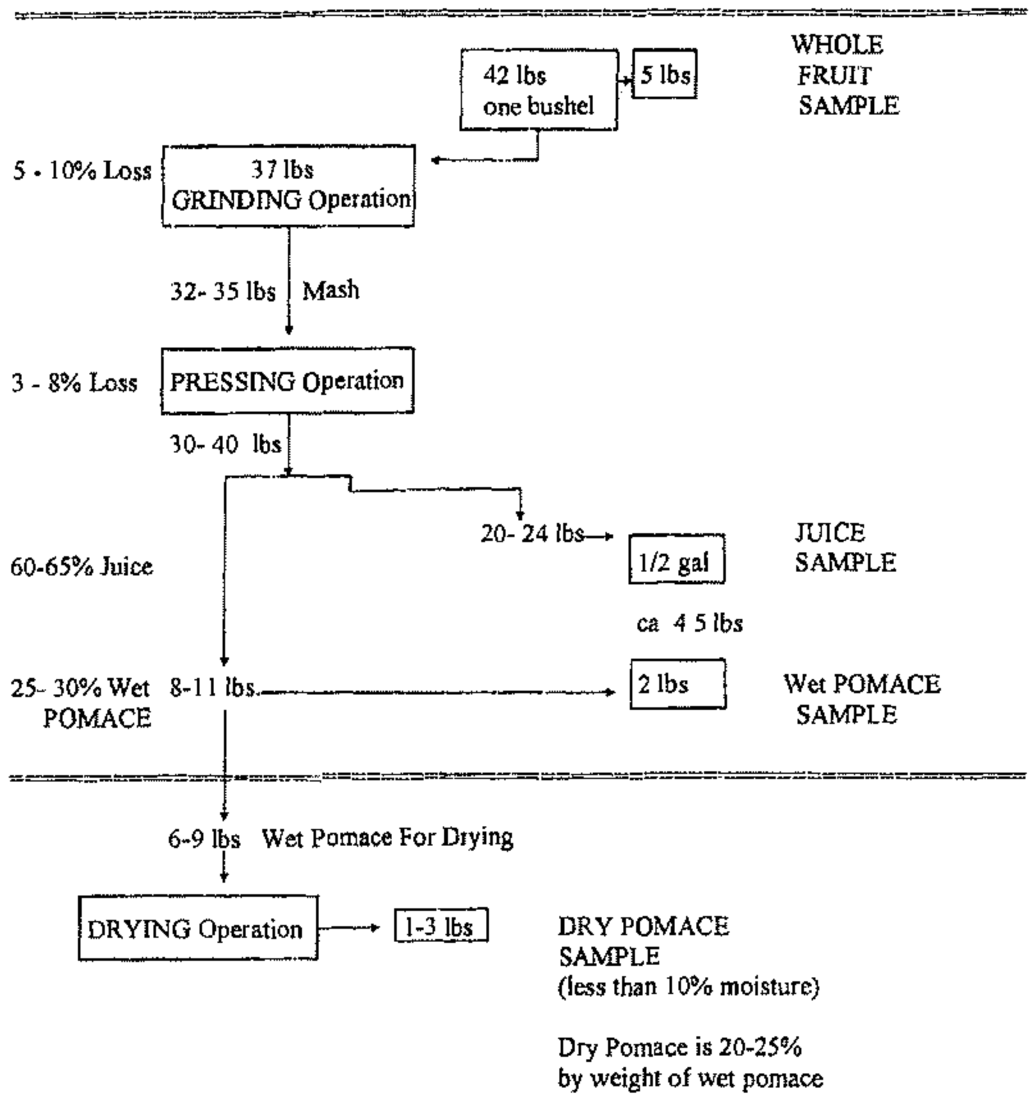
Figure B.1. Processing Flowchart for Apple Fruits.

A C D S. Research, Inc

FLOW CHART

Typical Small Batch Apple Processing Simulating Commercial Processing

Whole Fruit, Juice, Wet Pomace and Dry Pomace Fractions



B.3. Analytical Methodology

Residues of the free acid of endothall in/on apples and its processed fractions were determined using a LC/MS/MS method (Method No. KP-242R1) entitled "Analytical Method for Determination of Endothall in Crops", issued 5/4/2007.

For this method, residues in fruit and wet pomace were extracted twice by homogenization with water followed by centrifugation and filtering. The juice sample was just diluted with water. Residues were then derivatized with HFTH in 50% H_3PO_4 at 100-120°C for 90 minutes. After cooling, the derivatized residues were partitioned into MTBE, evaporated to dryness, and reconstituted in hexane:MTBE (1:1 v:v). Residues were then cleaned using an amine SPE cartridge eluted with methanol:MTBE (1:4). Residues were analyzed by LC/MS/MS using external standards. The m/z 397→166 ion transition was used for quantifying residues, and residues are expressed in acid equivalents. The validated LOQ for endothall is 0.05 ppm, and the estimated LOD was 0.0025 ppm.

For method validation, control samples of apple fruit were fortified with endothall at 0.05-5.0 ppm. For concurrent recoveries, control sample were fortified with endothall at 0.05-1.0 ppm for whole fruit and each processed fraction.

C. RESULTS AND DISCUSSION

The LC/MS/MS method used for determining residues of endothall in/on apples and its processed fractions was adequately validated prior to and in conjunction with the analysis of processing study samples (Table C.1). Method validation recoveries averaged (±SD) 88 ± 10% from whole fruit. Concurrent recoveries averaged 87% for whole fruit, 92% for juice, and 99% for wet pomace. Apparent residues of endothall were <LOQ in/on control samples of each matrix. Adequate sample calculations and example chromatograms were provided and the fortification levels used for method recoveries were similar in magnitude to the measured residue levels.

Apples were stored at -18°C for up to 230 days prior to analysis, and the processed fractions were stored at -18°C for up to 286 days prior to analysis (Table C.2). Adequate storage stability data are available indicating that endothall is stable in frozen tomatoes for up to 467 days (47520719.der, under review). These stability data will support the storage durations and conditions for the processing study.

Residues of endothall averaged 0.033 ppm in/on whole fruit (<LOQ) and were 0.041 ppm in juice and 0.091 ppm in wet pomace (Table C.3). The calculated processing factors were 1.2x for juice and 2.8x for wet pomace.

TABLE C.1. Summary of Method Validation and Concurrent Recoveries of Endothall from Apple and Its Processed Fractions.

Matrix	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean ± Std. Dev. [1] (%)
Method Validation				
Apple	0.05	3	91, 93, 93	92 ± 1
	0.5	3	76, 75, 74	75 ± 1
	5.0	3	92, 104, 94	97 ± 6
	Total	9	74-104	**88 ± 10**
Concurrent Recoveries				
Apple, fruit	0.05	2	75, 102	89
	0.5	1	77	77
	1.0	1	95	95
	Total	4	75-102	87 ± 13
Apple, juice	0.05	1	87	92
	1.0	1	96	
Apple, wet pomace	0.05	1	102	99
	1.0	1	95	

[1] Standard deviations are calculated for data sets having ≥3 values.

TABLE C.2. Summary of Storage Conditions for Apple Matrices.

Matrix	Storage Temperature (°C)	Actual Storage Duration (days)[1]	Interval of Demonstrated Storage Stability (days)[2]
Whole fruit	≤-18	230	467
Juice		231	
Wet pomace		286	

[1] Interval from harvest to extraction for analysis. Extracts were stored 1-6 days prior to analysis.
[2] Endothall is stable in frozen tomatoes for up to 467 days (47520719.der under review).

TABLE C.3. Residue Data from Apple Processing Study with Endothall.

RAC	Processed Commodity	Total Rate [1]	PHI (days)	Residues (ppm) [2]	Processing Factor [3]
Apple	Whole fruit roots (RAC)	5 ppm (6.79 lb ae/A)	0	(0.031, 0.047, 0.022) ave. 0.033	--
	Juice			(0.041)	1.2x
	Wet pomace			0.091	2.8x

[1] The rate is expressed both in terms of the concentration in the irrigation water (ppm) and the total amount (lb ae/A) applied.
[2] Expressed in acid equivalents. The LOQ is 0.05 ppm and the LOD estimated to be 0.0025 ppm. Values <LOQ but ≥LOD are listed in parentheses.
[3] Values <LOQ but ≥LOD were used for calculating processing factors

D. CONCLUSION

The apple processing study is adequate. Endothall residues concentrated slightly (1.2x) in juice and by 2.8x in wet pomace.

E. REFERENCES

None

F. DOCUMENT TRACKING

RDI: David Soderberg (5 June 2009); William Donovan (5 June 2009)
Petition Number: 8E7419
DP#: 356315
PC Code: 038901 and 038905

Template Version June 2005

Primary Evaluator	David Soderberg, Chemist, RABV, HED	Date: 5 June 2009
Approved by	William Donovan, Senior Scientist, RABV, HED	Date: 5 June 2009

This DER was originally prepared under contract by Dynamac Corporation (1910 Sedwick Road, Building 100, Suite B, Durham, NC 27713; submitted 3/27/2009). The DER has been reviewed by the Health Effects Division (HED) and revised as needed for clarity, correctness and to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORT:

47520710. Arsenovic, M. (2008) Endothall (Hydrothol 191 and Aquathol K): Magnitude of the Residue on Fruit Stone Group: Lab Project Number: Z9769, Z9769.07-ALS04, Unpublished study prepared by Interregional Research Project No. 4. 188 pages.

EXECUTIVE SUMMARY:

Interregional Research Project No. 4 (IR-4) submitted field trial data reflecting the exposure of peaches to endothall through the use of treated irrigation water. Two peach field trials were conducted in Zones 2 and 10 during 2007. In each trial, side-by-side tests were conducted using irrigation water treated with either the monoalkylamine salt of endothall (2 lb ae/gal SC/L) at a concentration of 5 ppm ae, or the dipotassium salt of endothall (3.0 lb ae/gal SC/L) at a concentration of 3.5 ppm ae. [In order to avoid the complications of different molecular weights for different salts, endothall concentrations are expressed as the free acid equivalents (ae).] The treated water was applied in each test during fruit development as six broadcast foliar applications using overhead sprinklers, at retreatment intervals (RTIs) of 6-8 days. A volume equivalent to ~1 acre inch of water (~27,154 gal/A) was applied for each application. Based on the endothall concentration and the amount of water applied, the application rate for the monoalkylamine salt of endothall was equivalent to 1.13-1.25 lb ae/A/application, for a total of 6.78-7.08 lb ae/A/season. The application rate for the dipotassium salt was equivalent to 0.79-0.91 lb ae/A/application, for a total of 4.82-5.05 lb ae/A/season.

Single control and duplicate treated samples of peaches were harvested from each test on the day of the final application (0 days after treatment, DAT), and samples were stored at ≤-10°C for up to 154 days prior to analysis. Adequate storage stability data are available to support the duration and conditions of sample storage.

Residues of endothall (free acid) in/on peaches were determined using an adequate LC/MS/MS method (Method No. KP-242R1). For this method, residues were extracted with water and then derivatized with heptafluoro-*p*-tolylhydrazine (HFTH) in 50% H_3PO_4. The derivatized residues were cleaned up by partitioning into methyl t-butyl ether (MTBE) followed by elution through an amine solid phase extraction (SPE) cartridge. Residues were then analyzed by LC/MS/MS using

external standards for quantitation. Residues are expressed in endothall acid equivalents. The validated limit of quantitation (LOQ) for endothall in/on peaches is 0.05 ppm, and the estimated limit of detection (LOD) is 0.0025 ppm.

Endothall residues were <0.05-0.160 ppm in/on 4 peach samples harvested at 0 DAT following irrigation applications of the monoalkylamine salt of endothall at 5 ppm ae, and were <0.05-0.136 ppm in/on 4 peach samples harvested at 0 DAT following six irrigation applications of the dipotassium salt of endothall at 3.5 ppm. Average endothall residues in/on peaches were 0.101 and 0.089 ppm for the monoalkylamine and dipotassium salt formulations, respectively. The highest average field trial (HAFT) residues were 0.152 and 0.127 ppm for the monoalkylamine and dipotassium salt formulations, respectively.

Although average endothall residues were lower (0.8x) for the dipotassium salt than the monoalkylamine salt, direct comparison of the two formulations is not appropriate because the two formulations were applied at different rates. The monoalkylamine salt was applied at 5 ppm acid equivalents; however, the dipotassium salt was applied at only 3.5 ppm acid equivalent, 0.7x the rate of the monoalkylamine salt. Although the dipotassium salt of endothall was applied according to label directions, using a concentration of 5 ppm ai for the irrigation water, this application rate did not take into account the acid equivalency of the dipotassium salt.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the peach field trial residue data for the monoalkylamine salt formulation are scientifically acceptable. Although limited field trials were performed, these applications are expected to be conservative relative to actual inadvertent applications. However, the field trial data for the dipotassium salt are not appropriate for direct comparison with the monoalkylamine salt because the dipotassium was applied at 0.7x the rate of the monoalkylamine salt. The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document, DP# 356315.

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported which would have an adverse impact on the validity of the study.

A. BACKGROUND INFORMATION

Endothall [7-oxabicyclo[2,2,1] heptane-2,3-dicarboxylic acid] is a selective contact herbicide, defoliant, desiccant, and aquatic algaecide that belongs to the dicarboxylic acid chemical class. The free acid of endothall (PC Code 038901) and its dipotassium (PC Code 038904) and alkylamine (PC Code 038905) salts are registered primarily as aquatic herbicides for the control a variety of plants in water bodies. This includes irrigation canals, but only with a 7 day holding period. They are also registered for desiccation/ defoliation of alfalfa/clover (grown for seed only), cotton, and potatoes prior to harvest, and for reduction of sucker branch growth in hops.

Permanent tolerances are established for the combined residues of endothall and its monomethyl ester at 0.1 ppm in/on cotton seeds, fish, dried hops and potatoes, and at 0.05 ppm in/on rice grain and straw [40 CFR §180.293(a)(1)].

In conjunction with a petition for tolerances on a wide variety of irrigated crops (PP# 8E7419), IR-4 has submitted field trial data reflecting irrigation of peaches with endothall-treated water. The chemical structure and nomenclature of endothall and its salts are listed in Table A.1. The physicochemical properties of technical grade endothall and its salts are listed in Table A.2.

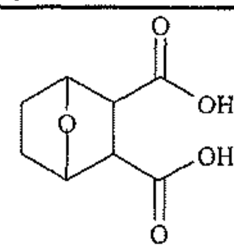
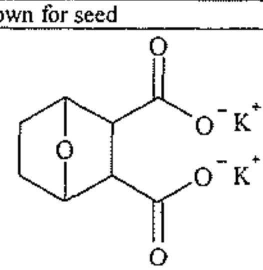
Table A.1. Structure and Nomenclature of Endothall and its Salts.	
Chemical Structure	
Common name	Endothall
Molecular Formula	$C_8H_{10}O_5$
Molecular Weight	186.16
IUPAC name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid
CAS name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid
CAS #	145-73-3
PC Code	038901
Current Food/Feed Site Registration	Cotton, hops, potato, alfalfa grown for seed
Chemical Structure	
Common name	Endothall, dipotassium salt
Molecular Formula	$C_8H_8K_2O_5$
Molecular Weight	262.33
IUPAC name	Not available
CAS name	Not available
CAS #	2164-07-0
PC Code	038904
Current Food/Feed Site Registration	Cotton, hops, potato, alfalfa grown for seed, aquatic uses

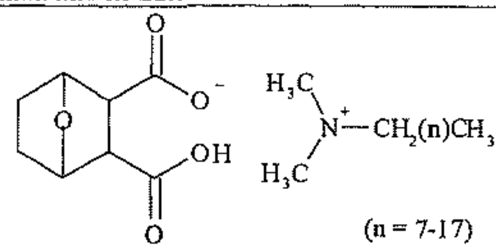
Table A.1. Structure and Nomenclature of Endothall and its Salts.	
Chemical Structure	 (n = 7-17)
Common name	Endothall, mono-N,N-dimethylalkyl amine salt
Molecular Formula	Not available
Molecular Weight	Average: 422
IUPAC name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid, compound with N,N-dimethylcocoamine
CAS name	Not available
CAS #	66330-88-9
PC Code	038905
Current Food/Feed Site Registration	Cotton, hops, potato, alfalfa grown for seed, aquatic uses

Table A.2. Physicochemical Properties of Endothall and Salts.

Parameter	Value	Reference
Endothall (acid)		
Melting point	108-110°C	D187593, D187590, and D187588, 5/5/93, K. Dockter
pH	2.7 at 25°C (1% solution)	D187593, D187590, and D187588, 5/5/93, K. Dockter
Density, bulk density, or specific gravity	0.481 g/cm^3 (bulk) at 25°C	D187593, D187590, and D187588, 5/5/93, K. Dockter
Water solubility at 25°C	109.8 g/L 13.1 g/100 mL in water, pH 5 12.7 g/100 mL in water, pH 7 12.5 g/100 mL in water, pH 9	D166798, 7/2/92, K. Dockter D207011, 9/30/94, F. Toghrol
Solvent solubility at 25°C	3.4 g/100 mL in acetonitrile 2.4 g/100 mL in n-octanol 16.0 g/100 mL in tetrahydrofuran	D207011, 9/30/94, F. Toghrol
Vapor pressure	3.92 x 10^{-5} mm Hg at 24.3°C	D166798, 7/2/92, K. Dockter
Dissociation constant, pK_a	4.32 for Step 1 and 6.22 for Step 2 at 20°C (0.2% solution in 20% basic ethanol); dissociation rate 1.8-2.3 x 10^3 μmho within 3-5 minutes at □25°C, by conductivity meter	D188708, 5/3/93, K. Dockter
Octanol/water partition coefficient	Not applicable to endothall acid	D166798, 7/2/92, K. Dockter
UV/visible absorption spectrum	Not available	
Endothall, dipotassium salt		
Melting point	>360°C	D187593, D187590, and D187588, 5/5/93, K. Dockter
pH	9.1 at 25°C (1% solution)	D187593, D187590, and D187588, 5/5/93, K. Dockter
Density, bulk density, or specific gravity	0.766 g/cm^3 (bulk) at 25°C	D187593, D187590, and D187588, 5/5/93, K. Dockter
Water solubility	>65 g/100 mL in water, pH 5, pH 7, and pH 9	D214691, 6/7/95, D. Hrdy
Solvent solubility	<0.001 g/100 mL in acetonitrile, n-octanol, and tetrahydrofuran	D214691, 6/7/95, D. Hrdy
Vapor pressure	Not applicable. An organic acid K salt is anticipated to have an insignificant vapor pressure.	D178085, 6/18/92, S. Funk

Table A.2. Physicochemical Properties of Endothall and Salts.		
Parameter	Value	Reference
Dissociation constant, pK_a	4.16 for Step 1 and 6.14 for Step 2 at 20℃ in water; dissociation complete at 5 mins (13.6 x 10^3 µmho)	D304027, 6/10/2004, D. Soderberg
Octanol/water partition coefficient	K_{OW} <0.02 and <0.3 at concentrations of 9 x 10^{-3} M and 9 x 10^{-4} M, respectively, at 25℃	D210814, 8/9/95, S. Knizner
UV/visible absorption spectrum	Not available	
Endothall, mono-N,N-dimethylalkyl amine salt		
Boiling point	Not available	
pH	5.2 at 25℃ (1% solution)	D187593, D187590, and D187588, 5/5/93, K. Dockter
Density, bulk density, or specific gravity	1.028 g/mL at 25℃	D187593, D187590, and D187588, 5/5/93, K. Dockter
Water solubility at 25℃	≥49.2 g/100mL in water, pH 5 ≥51.6 g/100 mL in water, pH 7 ≥49.8 g/100 mL in water, pH 9	D210814, 8/9/95, S. Knizner
Solvent solubility at 25℃	≥102.5 g/100mL in acetonitrile ≥95.4 g/100 mL in n-octanol ≥104.3 g/100 mL in tetrahydrofuran	D210814, 8/9/95, S. Knizner
Vapor pressure	2.09 x 10^{-5} mm Hg at 25℃ (calculated; mixed mono- and dialkylamine (C8-C20))	D206344, 9/22/94, F. Toghrol
Dissociation constant, pK_a	4.24 for Step 1 and 6.07 for Step 2 at 20℃ for mixed mono- and dialkylamine (C8-C20) in acidified ethanol/water; dissociation complete □17 minutes (1.7 x 10^3 µmho) at 25℃	D198885, 4/7/94, F. Toghrol
Octanol/water partition coefficient	K_{OW} 2.097 at concentrations of 8.9 x 10^{-3} M and 8.9 x 10^{-4} M, at 25℃	D209995, 1/20/95, L. Edwards
UV/visible absorption specrum	Not available	

B. EXPERIMENTAL DESIGN

B.1. Study Site Information

Two peach field trials were conducted in Zones 2 and 10 during the 2007 growing season (Table B.1.1). At each site, side-by-side tests were conducted using irrigation water treated with either the monoalkylamine salt of endothall (2.0 lb ae/gal SC/L) at a concentration of 5 ppm, acid equivalent, or the dipotassium salt of endothall (3.0 lb ae/gal SC/L) at a concentration of 3.5 ppm, acid equivalent. HED notes that although the dipotassium salt was applied at a concentration of ~5 ppm ai, this rate is equivalent to a concentration of 3.5 ppm, acid equivalent. The treated water was applied in each test during fruit development and maturation as six broadcast foliar applications using overhead sprinklers, at RTIs of 7-8 days. A volume equivalent to ~1 acre inch of water (~27,154 gal/A) was applied for each application. Based on the concentration of the endothall and the amount of water applied, the application rates for the monoalkylamine salt of endothall were equivalent to 1.13-1.25 lb ae/A/application, for a total of 6.78-7.08 lb ae/A/season (Table B.1.3). The application rates for the dipotassium salt were equivalent to 0.79-0.91 lb ae/A/application, for a total of 4.82-5.05 lb ae/A/season. These applications are expected to be conservative relative to actual applications.

TABLE B.1.1. Trial Site Conditions.

Trial Identification (City, State; Year)	Soil characteristics[1]			
	Type	%OM	pH	CEC (meq/100g)
Morven, GA 2007 GA$01	Loamy Sand	0.75	5.3	3.0
Dinuba, CA 2007 CA$02	Loamy Sand	4.1	7.0	8.7

[1] These parameters are optional except in cases where their value affects the use pattern for the chemical.

TABLE B.1.2. Water Characterization.

Study site	Water characteristics				
	Type	Hardness/Salinity	pH	Turbidity	Dissolved OM
Morven, GA 2007 GA$01	Well	NR	NR	NR	NR
Dinuba, CA 2007 CA$02	Well	NR	NR	NR	NR

NR = not reported.

The actual temperature recordings and rainfall were typical for each site and no unusual weather conditions were reported. No additional irrigation was reported during the study period. The tests were conducted according to normal agricultural practices for the regions, and information was provided on maintenance pesticides and fertilizers used at each site. No information was provided on the characteristics of the water used for irrigation, other than the source (Table B.1.2).

TABLE B.1.3. Study Use Pattern.

Location (City, State; Year) Trial ID	End-Use Product[1]	Application Information					
		Method; Timing	Concen.[2]	Volume (gal/A)[3]	Single Rate[4] (lb ae/A)	RTI[5] (days)	Total Rate[4] (lb ae/A)
Morven, GA 2007 GA$01	2.0 lb/gal SC	Six overhead sprinkler applications during fruit development and maturation	4.99-5.01	27,222-29,959	1.13-1.25	7	7.08
	3.0 lb/gal SC	Six overhead sprinkler applications during fruit development and maturation	3.5	27,011-29,803	0.79-0.91	7	5.05
Dinuba, CA 2007 CA$02	2.0 lb/gal SC	Six overhead sprinkler applications during fruit development and maturation	5.0	27,172-27,271	1.13	6-8	6.78
	3.0 lb/gal SC	Six overhead sprinkler applications during fruit development and maturation	3.5	27,172-27,271	0.80	6-8	4.82

[1] The two formulations used are expressed in lb acid equivalent/gal. The monoalkylamine salt is a 2.0 lb ae/gal SC/L and the dipotassium salt is a 3.0 lb ae/gal SC/L. When applied according to the label directions, the maximum concentration for endothall (free acid) is 5 ppm for the monoalkylamine salt and 3.5 ppm for the dipotassium salt.
[2] The concentration of endothall (in acid equivalents) in the irrigation water. No adjuvants were included in the irrigation water.
[3] The target irrigation rate was 1 acre inch of water or 27,154 gal/A.
[4] The equivalent field use rates were calculated by the reviewer based on the concentration of the endothall (ae), the application volume and plot size.
[5] RTI = Retreatment Interval.

TABLE B.1.4. Trial Numbers and Geographical Locations.

NAFTA Growing Zones [3]	Peaches		
	Submitted	Requested[1]	
		Canada	U.S.
1	--	--	1
2	1	--	4
3	--	--	--
4	--	--	1
5	--	--	1
6	--	--	1
7	--	--	--
8	--	--	--
9	--	--	--
10	1	--	4
11	--	--	--
12	--	--	--
13	--	--	--
Total	2	--	12 [9][2]

[1] Based on EPA OPPTS Guideline 860.1500.
[2] The number in brackets indicates a 25% reduction required to support a crop group tolerance.
[3] Zones 1A, 5 A and B, 7A and 14-21 were not included as the proposed use is for the U.S. only.

B.2. Sample Handling and Preparation

Duplicate control and treated samples (≥4.2 lb/sample, 24 fruits) of peaches were harvested at 0 DAT (after the sixth application) and placed in frozen storage at the test facilities within 3.5 hours. Samples were stored frozen at the field sites for 31-42 days prior to shipment by ACDS Freezer truck to the analytical laboratory, ALS Laboratory Group (Edmonton, AB, Canada) where they were stored at ≤-10°C until analysis.

B.3. Analytical Methodology

Residues of endothall (free acid) in/on peaches were determined using a LC/MS/MS method (Method No. KP-242R1) entitled "Analytical Method for Determination of Endothall in Crops", issued 5/4/2007.

For this method, residues were extracted twice by homogenization with water followed by centrifugation and filtering. Residues were then derivatized with HFTH in 50% H_3PO_4 at 100-120°C for 90 minutes. After cooling, the derivatized residues were partitioned into MTBE, evaporated to dryness, and reconstituted in hexane:MTBE (1:1 v:v). Residues were then cleaned using an amine SPE cartridge eluted with methanol. Residues were analyzed by LC/MS/MS using external standards. The m/z 397→166 ion transition was used for quantifying residues. Residues are expressed in endothall acid equivalents. The validated LOQ for endothall in/on peaches is 0.05 ppm, and the estimated LOD was 0.0025 ppm.

The above method was validated prior to and in conjunction with the analysis of the field trial samples. Control samples of peaches were fortified with endothall at 0.05-5.0 ppm for method validation and at 0.05 ppm for concurrent recoveries.

C. RESULTS AND DISCUSSION

The LC/MS/MS method used for determining residues of endothall in/on peaches was adequately validated prior to and in conjunction with the analysis of field trial samples. Method validation recovery averaged 104% with a standard deviation of 12%, and concurrent recoveries averaged 73% (Table C.1). Apparent residues of endothall were non-detectable in/on control samples. Adequate sample calculations and example chromatograms were provided and the fortification levels used for method recoveries were similar in magnitude to the measured residue levels.

Peach samples were stored frozen at ≤-10°C for up to 154 days prior to analysis (Table C.2). Adequate storage stability data are available indicating that endothall is stable in frozen tomatoes (acidic fruit) for up to 467 days (47520719.der, under review). These data will support the storage durations and conditions for the current field trials.

Following six overhead sprinkler applications with irrigation water containing the monoalkylamine salt of endothall at 5 ppm, acid equivalents (6.78-7.08 lb ae/A/season), endothall residues were <0.05-0.160 ppm in/on 4 samples of peaches harvested at 0 DAT (Table C.3). Average endothall residues were 0.101 ppm, and the HAFT residues were 0.152 ppm (Table C.4).

Following six overhead sprinkler applications with irrigation water containing the dipotassium salt of endothall at 3.5 ppm, acid equivalents (4.82-5.05 lb ae/A/season), endothall residues were <0.05-0.0.136 ppm in/on 4 samples of peaches harvested at 0 DAT. Average endothall residues were 0.089 ppm, and the HAFT residues were 0.127 ppm. No residue decline data was provided.

Although average endothall residues were lower (0.9x) for the dipotassium salt than the monoalkylamine salt, direct comparison of the two formulations is not possible as the two formulations were applied at different rates. As requested by HED, the monoalkylamine salt was applied at 5 ppm acid equivalents; however, the dipotassium salt was applied at only 3.5 ppm acid equivalent, 0.7x the rate of the monoalkylamine salt. Although the dipotassium salt of endothall was applied according to label directions, using a concentration of 5 ppm ai for the irrigation water, this application rate did not take into account the acid equivalency of the dipotassium salt.

Phytotoxicity was reported on the treated peach trees. Common cultural practices were used to maintain plants, and the weather conditions and maintenance chemicals and fertilizer used in this study did not have a notable impact on the residue data.

TABLE C.1. Summary of Method Validation and Concurrent Recoveries of Endothall from Peaches.

Matrix	Spike Level (ppm)	Sample Size (*n*)	Recoveries (%)	Mean ± Std. Dev. [1] (%)
Method Validation				
Fruit	0.05	3	91, 109, 87	96 ± 12
	0.5	3	98, 116, 121	112 ± 12
	5.0	3	97, 116, 106	106 ± 10
	Total	9	87-121	104 ± 12
Concurrent Recoveries				
Fruit	0.05	2	74, 72	73

[1] Standard deviations were calculated only for datasets having ≥3 values.

TABLE C.2. Summary of Storage Conditions.

Matrix	Storage Temperature (°C)	Actual Storage Duration (days)[1]	Interval of Demonstrated Storage Stability (days)[2]
Peaches	≤10	154	467

[1] Interval from harvest to extraction for analysis. Extracts were stored up to 4 days prior to analysis.
[2] Endothall is stable in frozen tomatoes for up to 467 days (47520719.der under review).

TABLE C.3. Residue Data from Peach Field Trials with Endothall Salts (SC/L).

Trial ID (City, State; Year)	Zone	Variety	Matrix	Total Rate		PHI (days)	Residues (ppm) [2, 3]	
				ppm	lb ae/A			
Morven, GA 2007 GA$01	2	White	Fruit	5.0	7.08	0	(0.045)	(0.043)
				3.5	5.05	0	(0.043)	(0.046)
Dinuba, CA 2007 CA$02	10	Snow Princess	Fruit	5.0	6.78	0	0.144	0.160
				3.5	4.82	0	0.118	0.136

[1] The rate is expressed both in terms of the concentration in the irrigation water (ppm) and the total amount (lb ae/A) applied. The application concentrations were 5 ppm ae for the monoalkylamine salt and 3.5 ppm ae for the dipotassium salt.
[2] Expressed in endothall acid equivalents. The LOQ is 0.05 ppm, and the estimated LOD is 0.0025 ppm. Residue <LOQ, but ≥LOD are listed in parentheses.
[3] The two results for each field trial represent two samples taken from a single plot, not two plots.

[redacted]

TABLE C.4. Summary of Residue Data from Peach Field Trials with Endothall Salts (SC/L).

Commodity	End-Use Product	Total Applic. Rate [1]	PHI (days)	Residue Levels (ppm) [2]						
				n	Min.	Max.	HAFT [3]	Median (STMdR)	Mean (STMR)	Std. Dev.
Fruit	Monoalkylamine salt (SC/L)	5 ppm (6.78-7.08)	0	2	0.044	0.152	0.152	0.098	0.098	0.076
Fruit	Dipotassium salt (SC/L)	3.5 ppm (4.82-5.05)	0	2	0.045	0.127	0.127	0.086	0.086	0.058

[1] The concentrations are expressed in acid equivalents, and the values in parentheses are the total application rate in terms of lb ae/A.
[2] Residues are expressed in terms of the free acid. The LOQ is 0.05 ppm. The LOQ was used for all values reported ≤LOQ.
[3] HAFT = Highest Average Field Trial.

D. CONCLUSION

The available field trial data are adequate and support the use of endothall-treated water for irrigation of peaches. The data support the use of the monoalkylamine salt of endothall in irrigation water at a concentration of 5 ppm ae and the use of the dipotassium salt of endothall in irrigation water at a concentration of 3.5 ppm ae. No more that six applications of treated water should be made per season with a minimum 7-day interval between applications to the water. Residues on peaches are determined at a 0-day PHI.

E. REFERENCES

None

F. DOCUMENT TRACKING

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Primary Evaluator	David Soderberg, Chemist, RABV, HED	Date: 5 June 2009
Approved by	William Donovan, Senior Scientist, RABV, HED	Date: 5 June 2009

This DER was originally prepared under contract by Dynamac Corporation (1910 Sedwick Road, Building 100, Suite B, Durham, NC 27713; submitted 3/27/2009). The DER has been reviewed by the Health Effects Division (HED) and revised as needed for clarity, correctness and to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORT:

47520711. Arsenovic, M. (2008) Endothall (Hydrothol 191): Magnitude of the Residue on Berry Group: Lab Project Number: Z9770. Unpublished study prepared by Interregional Research Project No. 4. 180 pages.

EXECUTIVE SUMMARY:

Interregional Research Project No. 4 (IR-4) submitted field trial data reflecting the exposure of blueberries and blackberries to endothall through the use of treated irrigation water. In a blueberry and blackberry field trial conducted during 2007 in Zones 5 and 11, respectively, a 2.0 lb ae/gal soluble concentrate (SC/L) formulation of endothall (monoalkylamine salt) was used to treat the irrigation water at a rate of 5 ppm. [In order to avoid the complications of different molecular weights for different salts, endothall concentrations are expressed as the free acid equivalents (ae).] The treated water was applied to the berry crops during fruit development and maturation as six broadcast foliar applications using overhead sprinklers, at retreatment intervals (RTIs) of 6-8 days. A volume equivalent to ~1 acre inch of water (27,154 gal/A) was applied for each application. Based on the concentration of the endothall and the amount of water applied, the application rates for endothall were equivalent to 1.12-1.13 lb ae/A/application, for a total of 6.73-6.77 lb ae/A/season.

Single control and duplicate treated samples of blueberries and blackberries were harvested from the respective tests on the day of the final application (0 days after treatment, DAT), and samples were stored at ≤-18°C for up to 98 days prior to analysis. Adequate storage stability data are available to support the duration and conditions of sample storage.

Residues of endothall (free acid) in/on berry samples were determined using an adequate LC/MS/MS method (Method No. KP-242R1). For this method, residues were extracted with water and then derivatized with heptafluoro-*p*-tolylhydrazine (HFTH) in 50% H_3PO_4. The derivatized residues were cleaned up by partitioning into methyl t-butyl ether (MTBE) and elution through an amine solid phase extraction (SPE) cartridge. Residues were then analyzed by LC/MS/MS using external standards for quantitation. Residues are expressed in endothall

acid equivalents. The validated limit of quantitation (LOQ) for endothall in/on berries is 0.05 ppm.

Following six overhead sprinkler applications with irrigation water containing endothall at 5 ppm (6.73-6.77 lb ae/A/season), endothall residues at 0 DAT were 0.158 and 0.197 ppm in/on 2 samples of blueberry and 0.311 and 0.346 ppm in/on 2 samples of blackberry. The average residues were 0.177 and 0.328ppm for blueberries and blackberries, respectively. No residue decline data was provided.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the berry field trial residue data are classified as scientifically acceptable. Although limited field trials were performed, these applications are expected to be conservative relative to actual inadvertent applications. The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document, DP# 356315.

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported which would have an adverse impact on the validity of the study.

A. BACKGROUND INFORMATION

Endothall [7-oxabicyclo[2,2,1] heptane-2,3-dicarboxylic acid] is a selective contact herbicide, defoliant, desiccant, and aquatic algaecide that belongs to the dicarboxylic acid chemical class. The free acid of endothall (PC Code 038901) and its dipotassium (PC Code 038904) and alkylamine (PC Code 038905) salts are registered primarily as aquatic herbicides for the control a variety of plants in water bodies. This includes irrigation canals, but only with a 7 day holding period. They are also registered for desiccation/ defoliation of alfalfa/clover (grown for seed only), cotton, and potatoes prior to harvest, and for reduction of sucker branch growth in hops. Permanent tolerances are established for the combined residues of endothall and its monomethyl ester at 0.1 ppm in/on cotton seeds, fish, dried hops and potatoes, and at 0.05 ppm in/on rice grain and straw [40 CFR §180.293(a)(1)].

In conjunction with a petition for tolerances on a wide variety of irrigated crops (PP# 8E7419), IR-4 has submitted field trial data reflecting irrigation of black berries and blueberries with endothall-treated water. The chemical structure and nomenclature of endothall and its monoalkylamine salt are listed in Table A.1. The physicochemical properties of technical grade endothall and its monoalkylamine salt are listed in Table A.2.

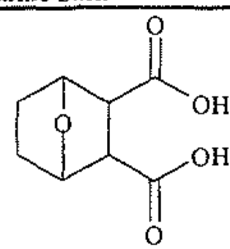
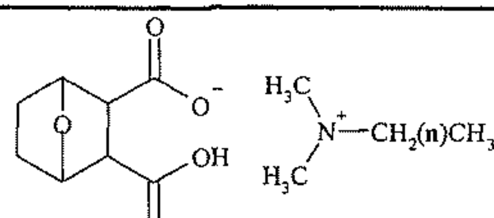
Table A.1. Nomenclature of Endothall and its Monoalkylamine Salt.	
Chemical Structure	
Common name	Endothall
Molecular Formula	$C_8H_{10}O_5$
Molecular Weight	186.16
IUPAC name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid
CAS name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid
CAS #	145-73-3
PC Code	038901
Current Food/Feed Site Registration	Cotton, hops, potato, alfalfa grown for seed
Chemical Structure	 (n = 7-17)
Common name	Endothall, mono-N,N-dimethylalkyl amine salt
Molecular Formula	Not available
Molecular Weight	Average: 422
IUPAC name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid, compound with N,N-dimethylcocoamine
CAS name	Not available
CAS #	66330-88-9
PC Code	038905
Current Food/Feed Site Registration	Cotton, hops, potato, alfalfa grown for seed, aquatic uses

Table A.2. Physicochemical Properties of Endothall and Its Monoalkylamine Salt.		
Parameter	Value	Reference
Endothall (acid)		
Melting point	108-110℃	D187593, D187590, and D187588, 5/5/93, K. Dockter
pH	2.7 at 25℃ (1% solution)	D187593, D187590, and D187588, 5/5/93, K. Dockter
Density, bulk density, or specific gravity	0.481 g/cm^3 (bulk) at 25℃	D187593, D187590, and D187588, 5/5/93, K. Dockter
Water solubility at 25℃	109.8 g/L 13.1 g/100 mL in water, pH 5 12.7 g/100 mL in water, pH 7 12.5 g/100 mL in water, pH 9	D166798, 7/2/92, K. Dockter D207011, 9/30/94, F. Toghrol
Solvent solubility at 25℃	3.4 g/100 mL in acetonitrile 2.4 g/100 mL in n-octanol 16.0 g/100 mL in tetrahydrofuran	D207011, 9/30/94, F. Toghrol
Vapor pressure	3.92 x 10^{-5} mm Hg at 24.3℃	D166798, 7/2/92, K. Dockter

Table A.2. Physicochemical Properties of Endothall and Its Monoalkylamine Salt.		
Parameter	Value	Reference
Dissociation constant, pK_a	4.32 for Step 1 and 6.22 for Step 2 at 20℃ (0.2% solution in 20% basic ethanol); dissociation rate 1.8-2.3 x 10^3 μmho within 3-5 minutes at □25℃, by conductivity meter	D188708, 5/3/93, K. Dockter
Octanol/water partition coefficient	Not applicable to endothall acid	D166798, 7/2/92, K. Dockter
UV/visible absorption spectrum	Not available	
Endothall, mono-N,N-dimethylalkyl amine salt		
Boiling point	Not available	
pH	5.2 at 25℃ (1% solution)	D187593, D187590, and D187588, 5/5/93, K. Dockter
Density, bulk density, or specific gravity	1.028 g/mL at 25℃	D187593, D187590, and D187588, 5/5/93, K. Dockter
Water solubility at 25℃	≥49.2 g/100mL in water, pH 5 ≥51.6 g/100 mL in water, pH 7 ≥49.8 g/100 mL in water, pH 9	D210814, 8/9/95, S. Knizner
Solvent solubility at 25℃	≥102.5 g/100mL in acetonitrile ≥95.4 g/100 mL in n-octanol ≥104.3 g/100 mL in tetrahydrofuran	D210814, 8/9/95, S. Knizner
Vapor pressure	2.09 x 10^{-5} mm Hg at 25℃ (calculated; mixed mono- and dialkylamine (C8-C20))	D206344, 9/22/94, F. Toghrol
Dissociation constant, pK_a	4.24 for Step 1 and 6.07 for Step 2 at 20℃ for mixed mono- and dialkylamine (C8-C20) in acidified ethanol/water; dissociation complete □17 minutes (1.7 x 10^3 μmho) at 25℃	D198885, 4/7/94, F. Toghrol
Octanol/water partition coefficient	K_{OW} 2.097 at concentrations of 8.9 x 10^{-3} M and 8.9 x 10^{-4} M, at 25℃	D209995, 1/20/95, L. Edwards
UV/visible absorption spectrum	Not available	

B. EXPERIMENTAL DESIGN

B.I. Study Site Information

Two field trials were conducted on blueberries and blackberries in Zones 5 and 11, respectively, during 2007 (Table B.1.1). The irrigation water used in each test was treated with endothall (2.0 lb ae/gal SC monoalkylamine salt) at a concentration of ~5 ppm, acid equivalent. The treated water was applied to each crop during fruit development and maturation as six broadcast foliar applications using overhead sprinklers, at RTIs of 6-8 days. A volume equivalent to ~1 acre inch of water (~27,000 gal/A) was applied for each application. Based on the concentration of the endothall and the amount of water applied, application rates for endothall were equivalent to 1.12-1.13 lb ae/A/application, for a total of 6.73-6.77 lb ae/A/season (Table B.1.3). These applications are expected to be conservative relative to actual applications.

TABLE B.1.1. Trial Site Conditions.				
Trial Identification (City, State; Year)	Soil characteristics[1]			
	Type	%OM	pH	CEC (meq/100g)
Conklin, MI 2007 MI$32	Loam	2.1	4.5	12.8
Hillsboro, OR 2007 OR$41	Silt Loam	2.9	6.0	12.8

[1]These parameters are optional except in cases where their value affects the use pattern for the chemical.

TABLE B.1.2. Water Characterization.					
Study site	Water characteristics				
	Type	Hardness/Salinity	pH	Turbidity	Dissolved OM
Conklin, MI 2007 MI$32	Well	NR	NR	NR	NR
Hillsboro, OR 2007 OR$41	Well	NR	NR	NR	NR

NR = not reported.

The actual temperature recordings and rainfall were typical for each site and no unusual weather conditions were reported. No additional irrigation was reported during the study period. The tests were conducted according to normal agricultural practices for the regions, and information was provided on maintenance pesticides and fertilizers used at each site. No information was provided on the characteristics of the water used for irrigation, other than the source (Table B.1.2).

TABLE B.1.3. Study Use Pattern.							
Location (City, State; Year) Trial ID	End-Use Product	Application Information					
		Method; Timing	Concen. [1]	Volume (gal/A) [2]	Single Rate (lb ae/A) [3]	RTI [4] (days)	Total Rate (lb ae/A) [3]
Blueberry							
Conklin, MI 2007 MI$32	2.0 lb/gal SC	Six broadcast foliar application during fruit development using overhead sprinklers.	4.98-5.00	27,154-27,160	1.13	7-8	6.77
Blackberry							
Hillsboro, OR 2007 OR$41	2.0 lb/gal SC	Six broadcast foliar application during fruit development using overhead sprinklers.	4.99-5.00	27,086	1.12	6-7	6.73

1 The concentration of endothall (in acid equivalents) in the irrigation water. No adjuvants were included in the irrigation water.
2 The target irrigation rate was 1 acre inch of water or 27,154 gal/A.
3 The equivalent field use rates were calculated by the reviewer based on the concentration of the endothall (ae), the application volume and plot size.
4 RTI = Retreatment Interval.

TABLE B.1.4. Trial Numbers and Geographical Locations.

NAFTA Growing Zones[2]	Blueberry (highbush)			Blackberry (or any raspberry)		
	Submitted	Requested[1]		Submitted	Requested[1]	
		Canada	U.S.		Canada	U.S.
1	--	--	1	--	--	--
2	--	--	2	--	--	1
3	--	--	--	--	--	--
4	--	--	--	--	--	--
5	1	--	2	--	--	--
6	--	--	--	--	--	1
7	--	--	--	--	--	
8	--	--	--	--	--	
9	--	--	--	--	--	
10	--	--	--	--	--	
11	--	--	--	--	--	
12	--	--	1	1	--	1
13	--	--	--	--	--	
Total	1	--	6	1	--	3

[1] Based on EPA OPPTS Guideline 860.1500. Indicates a 25% reduction for a crop group.
[2] Zones 1A, 5A and B, 7A and 14-20 were not included as the use is for U.S. only.

B.2. Sample Handling and Preparation

Blackberries and blueberries were harvested at 0 DAT (after the sixth application). Duplicate control and treated samples of berries (≥2.5 lbs/sample) were collected from each test and placed in frozen storage at each test facility within 1 hour. Samples were stored frozen at the field sites for 5-26 days. Samples were then shipped by ACDS freezer truck to the analytical laboratory, United Phosphorus, Inc. (King of Prussia, PA), and stored at ≤-18EC until analysis.

B.3. Analytical Methodology

Residues of endothall (free acid) in/on berries were determined using a LC/MS/MS method (Method No. KP-242R1) entitled "Analytical Method for Determination of Endothall in Crops", issued 5/4/2007.

For this method, residues were extracted twice by homogenization with water followed by centrifugation and filtering. Residues were then derivatized with HFTH in 50% H_3PO_4 at 100-120°C for 90 minutes. After cooling, the derivatized residues were partitioned into MTBE, evaporated to dryness, and reconstituted in hexane:MTBE (1:1 v:v). Residues were then cleaned using an amine SPE cartridge eluted with methanol:MTBE (1:4). Residues were analyzed by LC/MS/MS using external standards. The m/z 397→166 ion transition was used for quantifying residues. Residues are expressed in endothall acid equivalents. The validated LOQ for endothall in/on berries is 0.05 ppm. An LOD of 0.00001 ppm was reported; however, this value was the instrument LOD, rather than the LOD of residue in a control matrix.

The above method was validated prior to and in conjunction with the analysis of the field trial samples. Control samples of blackberries were fortified with endothall at 0.05-5.0 ppm for method validation, and control samples of blackberries and blueberries were fortified with endothall at 0.05-1.0 ppm for concurrent recoveries.

C. RESULTS AND DISCUSSION

The LC/MS/MS method used for determining residues of endothall in/on berries was adequately validated prior to and in conjunction with the analysis of field trial samples. The average method validation recovery was 93% with a standard deviation of 5% for blackberry (Table C.1). The average concurrent recovery was 85% for blueberry and 76% for blackberry. Apparent residues of endothall were <LOQ in/on control samples of berries. Adequate sample calculations and example chromatograms were provided, and the fortification levels used for the method recoveries were similar in magnitude to the measured residue levels.

Blueberry and blackberry samples were stored at <-18°C for up to 98 and 85 days, respectively, prior to analysis (Table C.2). Adequate storage stability data are available indicating that endothall is stable in frozen tomatoes for up to 467 days (47520719.der, under review). These data will support the storage durations and conditions for the current field trials.

Following six overhead sprinkler applications with irrigation water containing endothall at 5 ppm (6.73-6.77 lb ae/A/season), endothall residues at 0 DAT were 0.158 and 0.197 ppm in/on 2 samples of blueberry and 0.311 and 0.346 ppm in/on 2 samples of blackberry (Table C.3). The average residues were 0.177 ppm for blueberries and 0.328 ppm for blackberries (Table C.4). No residue decline data was provided.

No phytotoxicity was noted on the treated crops. Common cultural practices were used to maintain plants, and the weather conditions and maintenance chemicals and fertilizer used in this study did not have a notable impact on the residue data.

TABLE C.1. Summary of Method Validation and Concurrent Recoveries of Endothall from Berries

Matrix	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean ± Std. Dev. (%)
Method Validation				
Blackberry	0.05	3	93, 93, 93	93 ± 0
	0.5	3	92, 93, 103	96 ± 6
	5.0	3	85, 91, 94	90 ± 5
	Total	9	85-103	93 ± 5
Concurrent Recoveries				
Blueberry	0.05	1	83	83
	0.5	1	87	87
	Total	2	83-87	85
Blackberry	0.05	1	79	79
	1.0	1	73	73
	Total	2	73-79	76

Standard deviations are calculated for data sets having ≥3 values.

TABLE C.2. Summary of Storage Conditions.			
Matrix	Storage Temperature (°C)	Actual Storage Duration (days)[1]	Interval of Demonstrated Storage Stability (days)[2]
Blueberry	≤-18	98	467
Blackberry		85	

[1] Interval from harvest to extraction for analysis. Extracts were stored up to 1 day prior to analysis.
[2] Endothall is stable in frozen tomatoes for up to 467 days (47520719.der under review).

TABLE C.3. Residue Data from Crop Field Trials with Endothall Monoalkylamine Salt (SC/L).								
Trial ID (City, State; Year)	Zone	Crop; Variety	Matrix	Total Rate [1]		PHI (days)	Residues (ppm) [2, 3]	
				ppm	lb ae/A			
Conklin, MI 2007 MI$32	5	Blueberry: Blue Ray (Highbush)	Fruit	5.0	6.77	0	0.158	0.197
Hillsboro, OR 2007 OR$41	12	Blackberry (Boysen)	Fruit	5.0	6.73	0	0.311	0.346

[1] The rate is expressed both in terms of the concentration in the irrigation water (ppm) and the total amount (lb ae/A) applied.
[2] Expressed in acid equivalents. The LOQ is 0.05 ppm.
[3] The two results for each field trial represent two samples taken from a single plot, not two plots.

TABLE C.4. Summary of Residue Data from Berry Field Trials with Endothall Monoamine Salt (SC/L). FIX									
Commodity	Total Applic. Rate [1]	PHI (days)	Residue Levels (ppm) [2]						
			n	Min.	Max.	HAFT [3]	Median (STMdR)	Mean (STMR)	Std. Dev.
Blueberry	5.0 ppm (6.77)	0	1	0.177	0.177	0.177	0.177	0.177	N/A
Blackberry	5.0 ppm (6.73)	0	1	0.328	0.328	0.328	0.328	0.328	N/A

[1] The value in parentheses is the total application rate in terms of lb ae/A.
[2] Residues are expressed in terms of the free acid. The LOQ is 0.05 ppm
[3] HAFT = Highest Average Field Trial.

D. CONCLUSION

The available field trial data are adequate and support the use of endothall-treated water for irrigation of berry crops. The data support the use of endothall in irrigation water at a concentration of 5 ppm ae, with no more that six applications per season and a minimum 7-day interval between applications to the water. Residues on the berry crops were determined at a 0-day PHI.

E. REFERENCES

None

F. DOCUMENT TRACKING

RDI: David Soderberg (5 June 2009); William Donovan (5 June 2009)
Petition Number: 8E7419
DP#: 356315
PC Code: 038901 and 038905

Template Version June 2005

Primary Evaluator	David Soderberg, Chemist, RABV, HED	Date: 5 June 2009
Approved by	William Donovan, Senior Scientist, RABV, HED	Date: 5 June 2009

This DER was originally prepared under contract by Dynamac Corporation (1910 Sedwick Road, Building 100, Suite B, Durham, NC 27713; submitted 3/31/2009). The DER has been reviewed by the Health Effects Division (HED) and revised as needed for clarity, correctness and to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORT:

47520714. Arsenovic, M. (2008) Endothall (Hydrothol 191): Magnitude of the Residue on Grass, Forage, Fodder and Hay Group: Lab Project Number: Z9760. Unpublished study prepared by Interregional Research Project No. 4. 509 pages.

EXECUTIVE SUMMARY:

Interregional Research Project No. 4 (IR-4) submitted field trial data reflecting the exposure of grass to endothall through the use of treated irrigation water. A total of six grass field trials were conducted in Zones 4, 6, 11 and 12 during 2006 and 2007, including 2 field trials each on bluegrass, Bermuda and fescue grass. In each test, a 2.0 lb ae/gal soluble concentrate (SC/L) formulation of endothall (monoalkylamine salt) was used to treat the irrigation water at a rate of 5 ppm ae. [In order to avoid the complications of different molecular weights for different salts, endothall concentrations are expressed as the free acid equivalents (ae).] The treated water was applied to the grass during vegetative development as six broadcast foliar applications using overhead sprinklers, at retreatment intervals (RTIs) of 6-10 days. A volume equivalent to ~1 acre inch of water (27,154 gal/A) was applied for each application. Based on the concentration of the endothall in the irrigation water and the amount of water applied, the application rates for endothall were equivalent to 1.11-1.17 lb ae/A/application, for a total of 6.64-7.02 lb ae/A/season.

Duplicate control and treated samples of grass forage and hay were harvested on either the day of the final application (0 DAT) in the fescue tests, at 1 DAT in the Bermuda grass tests, or at 1-2 DAT in the bluegrass tests. The forage samples were collected immediately after harvest, and the hay samples were field-dried for 2-6 days prior to collection. After collection, samples were stored at ≤-10°C for up to 440 days prior to analysis. Adequate storage stability data are available to support the duration and conditions of sample storage.

Residues of endothall (free acid) in/on grass forage and hay were determined using an adequate LC/MS/MS method (Method No. KP-242R1). For this method, residues were extracted with water and then derivatized with heptafluoro-*p*-tolylhydrazine (HFTH) in 50% H_3PO_4. The derivatized residues were cleaned up by partitioning into methyl t-butyl ether (MTBE) and elution through an amine solid phase extraction (SPE) cartridge. Residues were then analyzed by LC/MS/MS using external standards for quantitation. Residues are expressed in endothall acid equivalents. The validated limit of quantitation (LOQ) for endothall in/on forage and hay is 0.05 ppm.

Following six overhead sprinkler applications with irrigation water containing endothall at 5 ppm (6.64-7.02 lb ae/A/season), endothall residues were 1.70-2.86 ppm in/on 12 forage samples and 5.34-14.2 ppm in/on 12 hay samples harvested at 0-2 DAT. Average endothall residues were 2.21 ppm for forage and 8.77 ppm for hay, and the highest average field trial (HAFT) residues were 2.73 ppm for forage and 13.65 ppm for hay. No residue decline data were provided.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the field trial residue data are classified as scientifically acceptable. Although limited field trials were performed, these applications are expected to be conservative relative to actual inadvertent applications. The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document, DP# 356315.

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported which would have an adverse impact on the validity of the study.

A. BACKGROUND INFORMATION

Endothall [7-oxabicyclo[2,2,1] heptane-2,3-dicarboxylic acid] is a selective contact herbicide, defoliant, desiccant, and aquatic algaecide that belongs to the dicarboxylic acid chemical class. The free acid of endothall (PC Code 038901) and its dipotassium (PC Code 038904) and alkylamine (PC Code 038905) salts are registered primarily as aquatic herbicides for the control a variety of plants in water bodies. , including irrigation canals. They are also registered for desiccation/ defoliation of alfalfa/clover (grown for seed only), cotton, and potatoes prior to harvest, and for reduction of sucker branch growth in hops. Permanent tolerances are established for the combined residues of endothall and its monomethyl ester at 0.1 ppm in/on cotton seeds, fish, dried hops and potatoes, and at 0.05 ppm in/on rice grain and straw [40 CFR §180.293(a)(1)].

In conjunction with a petition for tolerances on a wide variety of irrigated crops (PP# 8E7419), IR-4 has submitted field trial data reflecting irrigation of grass with endothall-treated water. The chemical structure and nomenclature of endothall and its monoalkylamine salt are listed in Table A.1. The physicochemical properties of technical grade endothall and its monoalkylamine salt are listed in Table A.2.

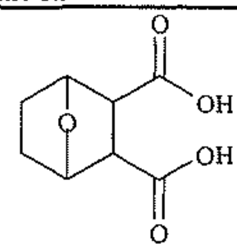
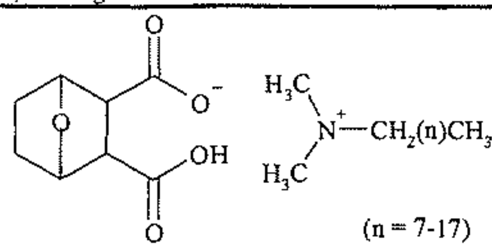
Table A.1. Nomenclature of Endothall and its Monoalkylamine Salt.	
Chemical Structure	
Common name	Endothall
Molecular Formula	$C_8H_{10}O_5$
Molecular Weight	186.16
IUPAC name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid
CAS name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid
CAS #	145-73-3
PC Code	038901
Current Food/Feed Site Registration	Cotton, hops, potato, alfalfa grown for seed
Chemical Structure	 (n = 7-17)
Common name	Endothall, mono-N,N-dimethylalkyl amine salt
Molecular Formula	Not available
Molecular Weight	Average: 422
IUPAC name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid, compound with N,N-dimethylcocoamine
CAS name	Not available
CAS #	66330-88-9
PC Code	038905
Current Food/Feed Site Registration	Cotton, hops, potato, alfalfa grown for seed, aquatic uses

Table A.2. Physicochemical Properties of Endothall and Its Monoalkylamine Salt.

Parameter	Value	Reference
Endothall (acid)		
Melting point	108-110°C	D187593, D187590, and D187588, 5/5/93, K. Dockter
pH	2.7 at 25°C (1% solution)	D187593, D187590, and D187588, 5/5/93, K. Dockter
Density, bulk density, or specific gravity	0.481 g/cm^3 (bulk) at 25°C	D187593, D187590, and D187588, 5/5/93, K. Dockter
Water solubility at 25°C	109.8 g/L 13.1 g/100 mL in water, pH 5 12.7 g/100 mL in water, pH 7 12.5 g/100 mL in water, pH 9	D166798, 7/2/92, K. Dockter D207011, 9/30/94, F. Toghrol
Solvent solubility at 25°C	3.4 g/100 mL in acetonitrile 2.4 g/100 mL in n-octanol 16.0 g/100 mL in tetrahydrofuran	D207011, 9/30/94, F. Toghrol
Vapor pressure	3.92 x 10^{-5} mm Hg at 24.3°C	D166798, 7/2/92, K. Dockter
Dissociation constant, pK$_a$	4.32 for Step 1 and 6.22 for Step 2 at 20°C (0.2% solution in 20% basic ethanol); dissociation rate 1.8-2.3 x 10^3 μmho within 3-5 minutes at □25°C, by conductivity meter	D188708, 5/3/93, K. Dockter
Octanol/water partition coefficient	Not applicable to endothall acid	D166798, 7/2/92, K. Dockter
UV/visible absorption spectrum	Not available	
Endothall, mono-N,N-dimethylalkyl amine salt		
Boiling point	Not available	
pH	5.2 at 25°C (1% solution)	D187593, D187590, and D187588, 5/5/93, K. Dockter
Density, bulk density, or specific gravity	1.028 g/mL at 25°C	D187593, D187590, and D187588, 5/5/93, K. Dockter
Water solubility at 25°C	≥49.2 g/100mL in water, pH 5 ≥51.6 g/100 mL in water, pH 7 ≥49.8 g/100 mL in water, pH 9	D210814, 8/9/95, S. Knizner
Solvent solubility at 25°C	≥102.5 g/100mL in acetonitrile ≥95.4 g/100 mL in n-octanol ≥104.3 g/100 mL in tetrahydrofuran	D210814, 8/9/95, S. Knizner
Vapor pressure	2.09 x 10^{-5} mm Hg at 25°C (calculated; mixed mono- and dialkylamine (C8-C20))	D206344, 9/22/94, F. Toghrol
Dissociation constant, pK$_a$	4.24 for Step 1 and 6.07 for Step 2 at 20°C for mixed mono- and dialkylamine (C8-C20) in acidified ethanol/water; dissociation complete □17 minutes (1.7 x 10^3 μmho) at 25°C	D198885, 4/7/94, F. Toghrol
Octanol/water partition coefficient	K_{OW} 2.097 at concentrations of 8.9 x 10^{-3} M and 8.9 x 10^{-4} M, at 25°C	D209995, 1/20/95, L. Edwards
UV/visible absorption spectrum	Not available	

B. EXPERIMENTAL DESIGN

B.1. Study Site Information

A total of six grass field trials were conducted in Zones 4, 6, 11, and 12 during 2006 and 2007, including two field trials each on bluegrass, Bermuda and fescue grasses (Table B.1.1). The irrigation water used in each test was treated with endothall (2.0 lb ae/gal SC monoalkylamine salt) at a concentration of ~5 ppm, acid equivalent. The treated water was applied to the grass during vegetative development as six broadcast foliar applications using overhead sprinklers, at

RTIs of 6-10 days. A volume equivalent to ~1 acre inch of water (~27,154 gal/A) was applied for each application. Based on the concentration of the endothall and the amount of water applied, application rates for endothall were equivalent to 1.11-1.17 lb ae/A/application, for a total of 6.64-7.02 lb ae/A/season (Table B.1.3). Although limited field trials were performed, these applications are expected to be conservative relative to actual inadvertent applications.

TABLE B.1.1. Trial Site Conditions.

Trial Identification (City, State; Year)	Soil characteristics[1]			
	Type	%OM	pH	CEC (meq/100g)
Lecompte, LA 2006 LA$12	Silt loam	0.6	7.6	11.7
East Bernard, TX 2006 TX$14	Clay	2.3	6.3	27.1
Ephrata, WA 2006 WA$15	Loamy sand	1.0	7.4	12.4
Newport, SR 2007 AR$37	Silt loam	1.6	6.6	7.9
Alexandria, LA 2006 LA$13	Silty clay loam	NR	NR	NR
Hillsboro, OR 2007 OR$38	Silt loam	2.3	6.3	16.0

[1]These parameters are optional except in cases where their value affects the use pattern for the chemical.

TABLE B.1.2. Water Characterization.

Study site	Water characteristics				
	Type	Hardness/Salinity	pH	Turbidity	Dissolved OM
Lecompte, LA 2006 LA$12	Well	NR	NR	NR	NR
East Bernard, TX 2006 TX$14	Well	NR	NR	NR	NR
Ephrata, WA 2006 WA$15	Well	NR	NR	NR	NR
Newport, SR 2007 AR$37	City water	NR	NR	NR	NR
Alexandria, LA 2006 LA$13	Well	NR	NR	NR	NR
Hillsboro, OR 2007 OR$38	Well	NR	NR	NR	NR

NR = not reported.

The actual temperature recordings and rainfall were typical for each site and no unusual weather conditions were reported. No irrigation was reported during the study period. The tests were conducted according to normal agricultural practices for the regions, and information was provided on maintenance pesticides and fertilizers used at each site. No information was provided on the characteristics of the water used for irrigation, other than the source (Table B.1.2).

TABLE B.1.3. Study Use Pattern.

Location (City, State; Year) Trial ID	End-Use Product	Application Information					
		Method; Timing	Concen. [1]	Volume (gal/A) [2]	Single Rate (lb ae/A) [3]	RTI [4] (days)	Total Rate (lb ae/A) [3]
Lecompte, LA 2006 LA$12	2.0 lb ae/gal SC/L	Six broadcast foliar application during vegetative development using overhead sprinklers.	5.0	28,212-28,291	1.17	6-7	7.02
East Bernard, TX 2006 TX$14	2.0 lb ae/gal SC/L	Six broadcast foliar application during vegetative development using overhead sprinklers.	5.0	27,078-27,114	1.13	6-8	6.75
Ephrata, WA 2006 WA$15	2.0 lb ae/gal SC/L	Six broadcast foliar application during vegetative development using overhead sprinklers.	5.0	26,715	1.11	7	6.64
Newport, SR 2007 AR$37	2.0 lb ae/gal SC/L	Six broadcast foliar application during vegetative development using overhead sprinklers.	5.0	27,152-27,173	1.13	7-10	6.76
Alexandria, LA 2006 LA$13	2.0 lb ae/gal SC/L	Six broadcast foliar application during vegetative development using overhead sprinklers.	5.0	28,257-28,272	1.17	6-7	7.00
Hillsboro, OR 2007 OR$38	2.0 lb ae/gal SC/L	Six broadcast foliar application during vegetative development using overhead sprinklers.	5.0	27,086	1.12	7	6.73

1 The concentration of endothall (in acid equivalents) in the irrigation water. No adjuvants were included in the irrigation water.
2 The target irrigation rate was 1 acre inch of water or 27,154 gal/A.
3 The equivalent field use rates were calculated by the reviewer based on the concentration of the endothall (ae), the application volume and plot size.
4 RTI = Retreatment Interval.

TABLE B.1.4. Trial Numbers and Geographical Locations.

NAFTA Growing Zones[3]	Grass		
	Submitted	Requested[1]	
		Canada	U.S.
1	--	--	--
2	--	--	--
3	--	--	--
4	3	--	--
5	--	--	--
6	1	--	--
7	--	--	--
8	--	--	--
9	--	--	--
10	--	--	--
11	1	--	--
12	1	--	--
13	--	--	--
Total	6	--	12 [2]

[1] Based on EPA OPPTS Guideline 860.1500.
[2] Guidelines do not specify zones for grass trials.
[3] Regions 1A, 5A and B, 7A and 14-21 are not included in this table as the proposed use is for the U.S. only.

B.2. Sample Handling and Preparation

Duplicate control and treated samples of forage (≥2.2 lb/samples) and hay (≥1.0 lb/samples) were harvested from each test site. The samples were cut at 0 DAT in the fescue tests, 1 DAT in the Bermuda grass tests, and 1-2 DAT in the bluegrass tests. The forage samples were frozen within 1.5 hours of collection, and the hay samples were field-dried for 2-6 days to a moisture content of 10-20% prior to collection and freezing. Samples were stored frozen at the field sites for 7-37 days. Samples were then shipped by ACDS freezer truck to the analytical laboratory, ALS Laboratory Group (Edmonton, AB, Canada), and stored frozen (≤-10EC) prior to analysis.

B.3. Analytical Methodology

Residues of endothall (free acid) in/on grass forage and hay were determined using a LC/MS/MS method (Method No. KP-242R1) entitled "Analytical Method for Determination of Endothall in Crops", issued 5/4/2007.

For this method, residues were extracted 2 or 3 times by homogenization with water followed by centrifugation and filtering. Residues were then derivatized with HFTH in 50% H_3PO_4 at 100-120°C for 90 minutes. After cooling, the derivatized residues were partitioned into MTBE, evaporated to dryness, and reconstituted in hexane:MTBE (1:1 v:v). Residues were then cleaned using an amine SPE cartridge eluted with methanol. Residues were analyzed by LC/MS/MS using external standards. The m/z 397→166 ion transition was used for quantifying residues. Residues are expressed in endothall acid equivalents. The validated LOQ for endothall in/on forage and hay is 0.05 ppm. An LOD of 0.000025 ppm was reported; however, this value was the instrument LOD, rather than the LOD of residues in a control matrix.

Control samples of forage and hay were fortified with endothall at 0.05-5.0 ppm for method validation and at 0.05-15.0 ppm for the concurrent recoveries.

C. RESULTS AND DISCUSSION

The LC/MS/MS method used for determining residues of endothall in/on grass forage and hay was adequately validated prior to and in conjunction with the analysis of field trial samples. The average method validation recoveries (±SD) were 92 ± 17% for forage and 86 ± 5% for hay (Table C.1). Average concurrent recoveries (±SD) were 92 ± 13% for forage and 86 ± 7% for hay. Apparent residues of endothall were <LOQ in/on all control samples of grasses. Adequate sample calculations and example chromatograms were provided, and the fortification levels used for the method recoveries were similar in magnitude to the measured residue levels.

Forage and hay samples were stored at <-10°C for up to 404 and 440 days, respectively, prior to analysis (Table C.2). Adequate storage stability data are available indicating that endothall is stable in frozen lettuce, corn grain and sugar beet roots for up to 465 days (47520719.der, under review). These stability data will support the storage durations and conditions for the current grass field trials.

Following six overhead sprinkler applications with irrigation water containing endothall at 5 ppm (6.64-7.02 lb ae/A/season), endothall residues were 1.70-2.86 ppm in/on 12 forage samples and 5.34-14.2 ppm in/on 12 hay samples harvested at 0-2 DAT (Table C.3). Average endothall residues were 2.21 ppm for forage and 8.77 ppm for hay, and the HAFT residues were 2.73 ppm for forage and 13.65 ppm for hay (Table C.4). No residue decline data were provided.

Phytotoxicity was reported in the treated plot at one field site (WA$15), and consisted of stunting and slight chlorosis. Common cultural practices were used to maintain plants, and the weather conditions and maintenance chemicals and fertilizer used in this study did not have a notable impact on the residue data.

TABLE C.1. Summary of Method Validation and Concurrent Recoveries of Endothall from Grass.

Matrix	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean ± Std. Dev. (%)
Method Validation				
Forage	0.05	6	76, 69, 64, 92, 83, 84	78 ± 11
	0.5	3	94, 100, 112	102 ± 9
	5.0	3	106, 110, 114	110 ± 4
	Total	**12**	**64-114**	**92 ± 17**
Hay	0.05	3	80, 82, 82	81 ± 1
	0.5	3	80, 88, 94	87 ± 7
	5.0	3	84, 88, 94	89 ± 5
	Total	9	80-94	86 ± 5
Concurrent Recoveries				
Forage	0.05	4	94, 89, 89, 72	86 ± 10
	0.5	3	78, 105, 75	86 ± 17
	5.0	1	93	93
	12.0	3	103, 107, 103	104 ± 2
	Total	**11**	72-107	92 ± 13
Hay	0.05	5	86, 91, 93, 92, 76	88 ± 7
	0.5	1	80	80
	5.0	2	78, 85	81
	8.0	1	79	79
	15.0	3	93, 87, 92	91 ± 3
	Total	**12**	**76-93**	86 ± 7

1 Standard deviations are calculated for data sets having ≥3 values.

TABLE C.2. Summary of Storage Conditions.

Matrix	Storage Temperature (°C)	Actual Storage Duration (days)[1]	Interval of Demonstrated Storage Stability (days)[2]
Forage	≤-10	404	469
Hay		440	

1 Interval from harvest to extraction for analysis. Extracts were stored up to 35 days prior to analysis.
2 Based on storage stability data from frozen tomatoes, lettuce, corn grain, sugar beet roots, and soybean seeds (47520719.der, under review).

TABLE C.3. Residue Data from Crop Field Trials with Endothall Monoalkylamine Salt (SC/L).

Trial ID (City, State; Year)	Zone	Crop; Variety	Matrix	Total Rate[1]		PHI[2] (days)	Residues (ppm)[3,4]	
				ppm	lb ae/A			
Lecompte, LA 2006 LA$12	4	Bermuda grass; Russell	Forage	5.0	7.02	1	2.08	2.23
			Hay				9.80	12.40
East Bernard, TX 2006 TX$14	6	Bermuda grass; Coastal	Forage	5.0	6.75	1	1.85	2.03
			Hay				13.1	14.2

TABLE C.3. Residue Data from Crop Field Trials with Endothall Monoalkylamine Salt (SC/L).

Trial ID (City, State; Year)	Zone	Crop; Variety	Matrix	Total Rate[1]		PHI[2] (days)	Residues (ppm)[3,4]	
				ppm	lb ae/A			
Ephrata, WA 2006 WA$15	11	Bluegrass; Kentucky	Forage	5.0	6.64	1	1.82	1.85
			Hay				7.17	8.91
Newport, SR 2007 AR$37	4	Bluegrass; Kentucky	Forage	5.0	6.76	2	2.65	2.81
			Hay				6.51	6.78
Alexandria, LA 2006 LA$13	4	Fescue; not available	Forage	5.0	7.00	0	1.70	2.86
			Hay				5.89	5.84
Hillsboro, OR 2007 OR$38	12	Fescue; Pure Gold	Forage	5.0	6.73	0	2.65	1.99
			Hay				5.34	9.24

1 The rate is expressed both in terms of the concentration in the irrigation water (ppm) and the total amount (lb ae/A) applied.
2 After cutting (harvest), the hay samples were field-dried for 2-6 days prior to collection.
3 Expressed in acid equivalents. The LOQ is 0.05 ppm.
4 The two results for each field trial represent two samples taken from a single plot, not two plots.

TABLE C.4. Summary of Residue Data from Grass Field Trials with Endothall Monoalkylamine Salt (SC/L).

Commodity	Total Applic. Rate[1]	PHI (days)	Residue Levels (ppm)[2]						
			N	Min.	Max.	HAFT[3]	Median (STMdR)	Mean (STMR)	Std. Dev.
Forage	5 ppm (6.64-7.02)	0-2	6	1.94	2.73	2.73	2.21	2.21	0.32
Hay		0-2	6	5.87	13.65	13.65	8.77	8.77	3.00

1 The value in parentheses is the total application rate in terms of lb ae/A.
2 Residues are expressed in terms of the free acid. The LOQ is 0.05 ppm.
3 HAFT = Highest Average Field Trial.

D. CONCLUSION

The available field trial data are adequate and support the use of endothall-treated water for irrigation of grasses. The data support the use of endothall in irrigation water at a concentration of 5 ppm ae, with no more that six applications per season, and a minimum 7-day interval between applications to the water. Residues on grasses are determined at PHIs of 0 days for forage and 1 day for hay.

E. REFERENCES

None

F. DOCUMENT TRACKING

RDI: David Soderberg (5 June 2009); William Donovan (5 June 2009)
Petition Number: 8E7419
DP#: 356315
PC Code: 038901 and 038905

Template Version June 2005

Primary Evaluator	David Soderberg, Chemist, RABV, HED	Date: 5 June 2009
Approved by	William Donovan, Senior Scientist, RABV, HED	Date: 5 June 2009

This DER was originally prepared under contract by Dynamac Corporation (1910 Sedwick Road, Building 100, Suite B, Durham, NC 27713; submitted 3/20/2009). The DER has been reviewed by the Health Effects Division (HED) and revised as needed for clarity, correctness and to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORT:

47520716. Arsenovic, M. (2008) Endothall (Hydrothol 191): Magnitude of the Residue on Grape: Lab Project Number: Z9754, Z9754.07-ALS02 Unpublished study prepared by Interregional Research Project No. 4. 272 pages.

EXECUTIVE SUMMARY:

Interregional Research Project No. 4 (IR-4) submitted field trial data reflecting the exposure of grapes to endothall through the use of treated irrigation water. In three grape field trials conducted in Zones 1, 10 and 11 during 2006 and 2007, a 2.0 lb ae/gal soluble concentrate (SC/L) formulation of endothall (monoalkylamine salt) was used to treat the irrigation water at a rate of 5 ppm ae. [In order to avoid the complications of different molecular weights for different salts, endothall concentrations are expressed as the free acid equivalents (ae).] The treated water was then applied using overhead sprinklers to the grapes as six broadcast foliar applications during fruit development at retreatment intervals (RTIs) of 6-8 days. A total of ~1 acre inch of water (27,154 gal/A) was applied for each application. Based on the concentration of the endothall and the amount of water applied, the application rates for endothall were equivalent to 1.11-1.13 lb ae/A/application, for a total of 6.64-6.76 lb ae/A/season.

Single control and duplicate treated samples of grapes were harvested on the day of the final application (0 days after treatment, DAT), and samples were stored at <-10°C for up to 379 days prior to analysis. Adequate storage stability data are available to support the duration and conditions of sample storage.

Residues of endothall (free acid) in/on grapes were determined using an adequate LC/MS/MS method (Method No. KP-242R1). For this method, residues were extracted with water and then derivatized with heptafluoro-*p*-tolylhydrazine (HFTH) in 50% H_3PO_4. The derivatized residues were cleaned up by partitioning into methyl t-butyl ether (MTBE) and elution through an amine solid phase extraction (SPE) cartridge. Residues were then analyzed by LC/MS/MS using external standards for quantitation. The validated limit of quantitation (LOQ) for endothall in/on grapes is 0.05 ppm, and the reported limit of detection (LOD) is 0.0001 ppm.

Following six overhead sprinkler applications of grapes with irrigation water containing endothall at 5 ppm (6.64-6.76 lb ae/A/season), endothall residues in/on grapes harvested at 0 DAT were 0.376-0.696 ppm. The average residues were 0.522 ppm and the highest average field trial (HAFT) residues were 0.642 ppm. No residue decline data was provided.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Although residue data are available from only three field trials, the grape field trial residue data are classified as scientifically acceptable. Although limited field trials were performed, these applications are expected to be conservative relative to actual inadvertent applications. The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document, DP# 356315.

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported which would have an adverse impact on the validity of the study.

A. BACKGROUND INFORMATION

Endothall [7-oxabicyclo[2,2,1] heptane-2,3-dicarboxylic acid] is a selective contact herbicide, defoliant, desiccant, and aquatic algicide that belongs to the dicarboxylic acid chemical class. The free acid of endothall (PC Code 038901) and its dipotassium (PC Code 038904) and alkylamine (PC Code 038905) salts are registered primarily as aquatic herbicides for the control a variety of plants in water bodies. , including irrigation canals. They are also registered for desiccation/defoliation of alfalfa/clover (grown for seed only), cotton, and potatoes prior to harvest, and for reduction of sucker branch growth in hops. Permanent tolerances are established for the combined residues of endothall and its monomethyl ester at 0. 1 ppm in/on cotton seeds, fish, dried hops and potatoes, and at 0.05 ppm in/on rice grain and straw [40 CFR §180.293(a)(1)].

In conjunction with a petition for tolerances on a wide variety of irrigated crops (PP# 8E7419), IR-4 has submitted field trial data reflecting irrigation of grapes with endothall-treated water. The chemical structure and nomenclature of endothall and its salts are listed in Table A.1. The physicochemical properties of technical grade endothall and its salts are listed in Table A.2.

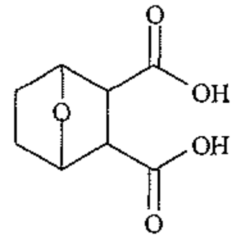
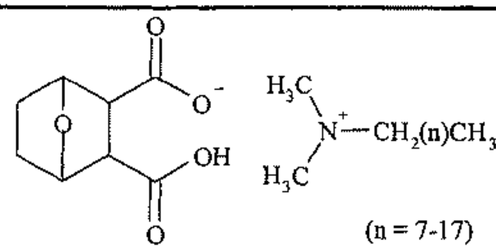
Table A.1. Endothall and Salts Nomenclature	
Chemical Structure	
Common name	Endothall
Molecular Formula	$C_8H_{10}O_5$
Molecular Weight	186.16
IUPAC name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid
CAS name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid
CAS #	145-73-3
PC Code	038901
Current Food/Feed Site Registration	Cotton, hops, potato, alfalfa grown for seed
Chemical Structure	 (n = 7-17)
Common name	Endothall, mono-N,N-dimethylalkyl amine salt
Molecular Formula	Not available
Molecular Weight	Average: 422
IUPAC name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid, compound with N,N-dimethylcocoamine
CAS name	Not available
CAS #	66330-88-9
PC Code	038905
Current Food/Feed Site Registration	Cotton, hops, potato, alfalfa grown for seed, aquatic uses

Table A.2. Physicochemical Properties of Endothall and Salts		
Parameter	Value	Reference
Endothall (acid)		
Melting point	108-110℃	D187593, D187590, and D187588, 5/5/93, K. Dockter
pH	2.7 at 25℃ (1% solution)	D187593, D187590, and D187588, 5/5/93, K. Dockter
Density, bulk density, or specific gravity	0.481 g/cm^3 (bulk) at 25℃	D187593, D187590, and D187588, 5/5/93, K. Dockter
Water solubility at 25℃	109.8 g/L 13.1 g/100 mL in water, pH 5 12.7 g/100 mL in water, pH 7 12.5 g/100 mL in water, pH 9	D166798, 7/2/92, K. Dockter D207011, 9/30/94, F. Toghrol
Solvent solubility at 25℃	3.4 g/100 mL in acetonitrile 2.4 g/100 mL in n-octanol 16.0 g/100 mL in tetrahydrofuran	D207011, 9/30/94, F. Toghrol
Vapor pressure	3.92×10^{-5} mm Hg at 24.3℃	D166798, 7/2/92, K. Dockter

Table A.2. Physicochemical Properties of Endothall and Salts		
Parameter	Value	Reference
Dissociation constant, pK_a	4.32 for Step 1 and 6.22 for Step 2 at 20℃ (0.2% solution in 20% basic ethanol); dissociation rate 1.8-2.3 x 10^3 μmho within 3-5 minutes at □25℃, by conductivity meter	D188708, 5/3/93, K. Dockter
Octanol/water partition coefficient	Not applicable to endothall acid	D166798, 7/2/92, K. Dockter
UV/visible absorption spectrum	Not available	
Endothall, mono-N,N-dimethylalkyl amine salt		
Boiling point	Not available	
pH	5.2 at 25℃ (1% solution)	D187593, D187590, and D187588, 5/5/93, K. Dockter
Density, bulk density, or specific gravity	1.028 g/mL at 25℃	D187593, D187590, and D187588, 5/5/93, K. Dockter
Water solubility at 25℃	≥49.2 g/100mL in water, pH 5 ≥51.6 g/100 mL in water, pH 7 ≥49.8 g/100 mL in water, pH 9	D210814, 8/9/95, S. Knizner
Solvent solubility at 25℃	≥102.5 g/100mL in acetonitrile ≥95.4 g/100 mL in n-octanol ≥104.3 g/100 mL in tetrahydrofuran	D210814, 8/9/95, S. Knizner
Vapor pressure	2.09 x 10^{-5} mm Hg at 25℃ (calculated; mixed mono- and dialkylamine (C8-C20))	D206344, 9/22/94, F. Toghrol
Dissociation constant, pK_a	4.24 for Step 1 and 6.07 for Step 2 at 20℃ for mixed mono- and dialkylamine (C8-C20) in acidified ethanol/water; dissociation complete □17 minutes (1.7 x 10^3 μmho) at 25℃	D198885, 4/7/94, F. Toghrol
Octanol/water partition coefficient	K_{OW} 2.097 at concentrations of 8.9 x 10^{-3} M and 8.9 x 10^{-4} M, at 25℃	D209995, 1/20/95, L. Edwards
UV/visible absorption spectrum	Not available	

B. EXPERIMENTAL DESIGN

B.1. Study Site Information

Three grape field trials were conducted in Zones 1, 10 and 11 during the 2006 and 2007 growing season (Table B.1.1). The irrigation water used in each test was treated with endothall (2.0 lb ae/gal SC monoalkylamine salt) at a concentration of ~5 ppm, acid equivalent. The treated water was then applied using overhead sprinklers to the grapes as six broadcast foliar applications during fruit development at RTIs of 6-8 days. A total of ~1 acre inch of water (27,154 gal/A) was applied for each application. Based on the concentration of the endothall and the amount of water applied, application rates for endothall were equivalent to 1.11-1.13 lb ae/A/application, for a total of 6.64-6.76 lb ae/A/season (Table B.1.3). These applications are expected to be very conservative relative to actual applications. [According to BEAD, grapes are only irrigated from overhead before fruiting occurs. One the fruit is set, only drip irrigation is used to avoid fungal infections of the fruit.]

TABLE B.1.1. Trial Site Conditions.

Trial Identification (City, State; Year)	Soil characteristics [1]			
	Type	%OM	pH	CEC (meq/100g)
North Rose, NY 2006 NY$01	Loamy Sand	2.7	6.6	7.4
San Luis Obispo, CA 2007 CA$31	Sandy Loam	1.9	6.2	17.6
Ephrata, WA 2006 WA$02	Sandy Loam	0.9	7.9	13.6

[1] These parameters are optional except in cases where their value affects the use pattern for the chemical.

TABLE B.1.2 Water Characterization.

Study site	Water characteristics				
	Type	Hardness/Salinity	pH	Turbidity	Dissolved OM
North Rose, NY 2006 NY$01	Well	NR	NR	NR	NR
San Luis Obispo, CA 2007 CA$31	Well	NR	NR	NR	NR
Ephrata, WA 2006 WA$02	Well	NR	NR	NR	NR

The actual temperature recordings and rainfall were typical for each site and no unusual weather conditions were reported. No additional irrigation was reported during the study period. The tests were conducted according to normal agricultural practices for the regions, and information was provided on maintenance pesticides and fertilizers used at each site. No information was provided on the characteristics of the water used for irrigation, other than the source (Table B.1.3).

TABLE B.1.3. Study Use Pattern.

Location (City, State; Year) Trial ID	End-Use Product	Application Information					
		Method; Timing	Concen. [1]	Volume (gal/A) [2]	Single Rate (lb ae/A) [3]	RTI [4] (days)	Total Rate (lb ae/A) [3]
North Rose, NY 2006 NY$01	2.0 lb ae/gal SC	Six broadcast foliar application during fruit development using overhead sprinklers.	4.98	26,998	1.12	7	6.73
San Luis Obispo, CA 2007 CA$31	2.0 lb ae/gal SC	Six broadcast foliar application during fruit development using overhead sprinklers.	4.98	26,715	1.13	6-8	6.76
Ephrata, WA 2006 WA$02	2.0 lb ae/gal SC	Six broadcast foliar application during fruit development using overhead sprinklers.	4.97	27,149	1.11	7	6.64

[1] The concentrate of endothall (in acid equivalents) in the irrigation water. No adjuvants were included in the irrigation water.
[2] The target irrigation rate was 1 acre inch of water or 27,154 gal/A.
[3] The equivalent field use rates were calculated by the reviewer based on the concentration of the endothall (ae), the application volume and plot size.
[4] RTI = Retreatment Interval.

TABLE B.1.4. Trial Numbers and Geographical Locations.

NAFTA Growing Zones [2]	Grapes		
	Submitted	Requested [1]	
		Canada	U.S.
1	1	--	2
2	--	--	--
3	--	--	--
4	--	--	--
5	--	--	--
6	--	--	--
7	--	--	--
8	--	--	--
9	--	--	--
10	1	--	8
11	1	--	1
12	--	--	1
13	--	--	--
Total	3	--	12

[1] Based on EPA OPPTS Guideline 860.1500.
[2] Zones 1A, 5 A and B, 7A and 14-21 were not included as the proposed use is for the U.S. only.

B.2. Sample Handling and Preparation

Duplicate control and treated samples of grapes (≥2 lbs/sample) were harvested at 0 DAT following the sixth application and placed in frozen storage at the test facility within 1 hour. Samples were stored frozen at the field sites for 5-34 days prior to shipment by freezer truck or overnight courier on dry ice to the analytical laboratory (ALS Laboratory Group, Edmonton, AB, Canada), where the samples were at ≤-10°C until analysis.

B.3. Analytical Methodology

Residues of the free acid of endothall in/on grapes were determined using a LC/MS/MS method (Method No. KP-242R1) entitled "Analytical Method for Determination of Endothall in Crops", issued 5/4/2007.

For this method, residues were extracted twice by homogenization with water followed by centrifugation and filtering. Residues were then derivatized with HFTH in 50% H_3PO_4 at 100-120°C for 90 minutes. After cooling, the derivatized residues were partitioned into MTBE, evaporated to dryness, and reconstituted in hexane:MTBE (1:1 v:v). Residues were then cleaned using an amine SPE cartridge eluted with methanol:MTBE (1:4). Residues were analyzed by LC/MS/MS using external standards. The m/z 397→166 ion transition was used for quantifying residues. The validated LOQ for endothall in/on grapes is 0.05 ppm, and the reported LOD is 0.0001 ppm.

The above method was validated prior to and in conjunction with the analysis of the grape field trial samples. Control samples were fortified with endothall at 0.05-5.0 ppm for method validation and for concurrent recoveries.

C. RESULTS AND DISCUSSION

The LC/MS/MS method used for determining residues of endothall in/on grapes was adequately validated prior to and in conjunction with the analysis of field trial samples. Method validation recovery averaged 90% with a standard deviation of 13%, and concurrent recoveries averaged 101% with a standard deviation of 19% (Table C.1). Apparent residues of endothall were non-detectable in/on control samples. Adequate sample calculations and example chromatograms were provided and the fortification levels used for method recoveries were similar in magnitude to the measured residue levels.

Grape samples were stored frozen at ≤-10°C for up to 379 days prior to analysis (Table C.2). Adequate storage stability data are available indicating that endothall is stable in frozen tomatoes for up to 467 days (47520719.der, under review). The stability data for tomatoes will support the storage durations and conditions for the current grape field trials.

Following six overhead sprinkler applications of endothall (monoalkylamine salt) to grapes at a rates totaling 6.64-6.76 lb ae/A, endothall residues in/on grapes harvested at 0 DAT were 0.376-0.696 ppm (Table C.3). The average residues were 0.522 ppm and the HAFT residues were 0.642 ppm (Table C.4). No residue decline data was provided.

Following six overhead sprinkler applications of grapes with irrigation water containing endothall at 5 ppm (6.64-6.76 lb ae/A/season), endothall residues in/on grapes harvested at 0 DAT were 0.376-0.696 ppm (Table C.3). The average residues were 0.522 ppm and the highest average field trial (HAFT) residues were 0.642 ppm (Table C.4). No residue decline data was provided.

Common cultural practices were used to maintain plants, and the weather conditions and maintenance chemicals and fertilizer used in this study did not have a notable impact on the residue data.

In both the NY and WA field trials, phytotoxicity was noted beginning with the second application and increased in severity with subsequent applications. The leaves initially showed signs of chlorosis and browning, with leaf necrosis occurring at later applications. No phytotoxicity was reported on the fruit, and not phytotoxicity was reported for the CA trial.

TABLE C.1. Summary of Method Validation and Concurrent Recoveries of Endothall from Grapes.				
Matrix	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean ± Std. Dev. (%)
Method Validation				
Fruit	0.05	3	74, 71, 76	74±3
	0.5	3	96, 102, 106	101 ± 5
	5.0	3	96, 95, 97	96 ± 1
	Total	9	71-106	90 ± 13
Concurrent Recoveries				
Fruit	0.05	2	95, 112	104
	5.0	2	76, 119	97
	Total	4	76-119	101 ± 19

TABLE C.2. Summary of Storage Conditions.			
Matrix	Storage Temperature (°C)	Actual Storage Duration (days)[1]	Interval of Demonstrated Storage Stability (days)[2]
Grape	≤-10	88-379	467

[1] Interval from harvest to extraction for analysis. Extracts were stored 3-22 days prior to analysis.
[2] Endothall is stable in frozen tomatoes for up to 467 days (47520719.der under review).

TABLE C.3. Residue Data from Grape Field Trials with Endothall (2 lb ae/gal SC/L).								
Trial ID (City, State; Year)	Zone	Variety	Matrix	Total Rate[1]		PHI (days)	Residues (ppm)[2, 3]	
				ppm	(lb ae/A)			
North Rose, NY 2006 NY$01	1	Elvira	Fruit	4.98	6.73	0	0.433	0.376
San Luis Obispo, CA 2007 CA$31	10	Pinot 155	Fruit	4.98	6.76	0	0.588	0.449
Ephrata, WA 2006 WA$02	11	Riesling	Fruit	4.97	6.64	0	0.587	0.696

[1] The rate is expressed both in terms of the concentration in the irrigation water (ppm) and the total amount (lb ae/A) applied.
[2] Expressed as the free acid. The LOQ is 0.05 ppm and the LOD is 0.0001 ppm.
[3]. The two results for each field trial represent two samples taken from a single plot, not two plots.

TABLE C.4. Summary of Residue Data from Grape Field Trials with Endothall.									
Commodity	Total Applic. Rate[1]	PHI (days)	Residue Levels (ppm)[2]						
			n	Min.	Max.	HAFT[3]	Median (STMdR)	Mean (STMR)	Std. Dev.
Grape	5.0 ppm (6.64-6.76)	0	3	0.405	0.642	0.642	0.522	0.522	0.119

[1] The value in parentheses is the total application rate in terms of lb ae/A.
[2] Residues are expressed in terms of the free acid. The LOQ is 0.05 ppm.
[3] HAFT = Highest Average Field Trial.

D. CONCLUSION

The available field trial data are adequate and support the use of endothall-treated water for irrigation of grapes. The data support the use of endothall in irrigation water at a concentration of 5 ppm ae, with no more that six applications per season and a minimum 7-day interval between applications to the water. Residues on the grapes are determined at a 0-day PHI.

E. REFERENCES

None

F. DOCUMENT TRACKING

RDI: David Soderberg (5 June 2009); William Donovan (5 June 2009);
Petition Number: 8E7419
DP#: 356315
PC Code: 038901, 038905

Template Version June 2005

Primary Evaluator	David Soderberg, Chemist, RABV, HED	Date: 5 June 2009
Approved by	William Donovan, Senior Scientist, RABV, HED	Date: 5 June 2009

This DER was originally prepared under contract by Dynamac Corporation (1910 Sedwick Road, Building 100, Suite B, Durham, NC 27713; submitted 3/20/2009). The DER has been reviewed by the Health Effects Division (HED) and revised as needed for clarity, correctness and to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORT:

47520716. Arsenovic, M. (2008) Endothall (Hydrothol 191): Magnitude of the Residue on Grape: Lab Project Number: Z9754, Z9754.07-ALS02 Unpublished study prepared by Interregional Research Project No. 4. 272 pages.

EXECUTIVE SUMMARY:

Interregional Research Project No. 4 (IR-4) submitted a grape processing study reflecting the exposure of grapes to endothall through the use of treated irrigation water. In a field trial conducted in NY (Zones 1) during 2006, a 2.0 lb ae/gal soluble concentrate (SC/L) formulation of endothall (monoalkylamine salt) was used to treat the irrigation water at a rate of 5 ppm ae. [In order to avoid the complications of different molecular weights for different salts, endothall concentrations are expressed as the free acid equivalents (ae).] The treated water was then applied using overhead sprinklers to the grapes as six broadcast foliar applications during fruit development at retreatment intervals of 7 days. A total of ~1 acre inch of water (27,154 gal/A) was applied for each application. Based on the concentration of the endothall and the amount of water applied, the application rates for endothall were equivalent to 1.12 lb ae/A/application, for a total of 6.73 lb ae/A/season.

Single bulk control and treated samples of grapes were harvested at normal crop maturity, immediately following the last irrigation (0 days after treatment, DAT). The grapes were processed into juice and raisins within 2 days for harvest using simulated commercial procedures. Grape juice was cold pressed and gave an unusually low yield. Whole fruit and processed fractions were stored frozen for up to 377 days prior to analysis. The sample storage intervals and conditions are supported by the available storage stability data.

Residues of endothall (free acid) in/on grapes and grape processed fractions were determined using an adequate LC/MS/MS method (Method No. KP-242R1). For this method, residues were extracted with water and then derivatized with heptafluoro-*p*-tolylhydrazine (HFTH) in 50% H_3PO_4. The derivatized residues were cleaned up by partitioning into methyl t-butyl ether (MTBE) and elution through an amine solid phase extraction (SPE) cartridge. Residues were then analyzed by LC/MS/MS using external standards for quantitation. The validated limit of

200

quantitation (LOQ) for endothall is 0.05 ppm, and the reported limit of detection (LOD) is 0.0001 ppm.

Residues of endothall averaged 0.280 ppm in/on whole grapes (RAC) were 1.24 ppm in juice and 1.21 ppm in raisins. The processing factors for juice and raisins were 4.3x and 4.4x, respectively. The theoretical concentration factors for juice and raisins are 1.2x and 4.7x, respectively. Although the processing factor for raisins was in line with the theoretical value, the processing factor for juice was impossibly higher than the maximum theoretical concentration factor.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the grape processing study is scientifically acceptable for processing to raisins. It is not acceptable for processing to grape juice. The juice was cold pressed when grape juice is normally hot pressed. The yield was unusually low, and the residue results were impossibly high. The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document, DP# 356315.

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported which would have an adverse impact on the validity of the study.

A. BACKGROUND INFORMATION

Endothall [7-oxabicyclo[2,2,1] heptane-2,3-dicarboxylic acid] is a selective contact herbicide, defoliant, desiccant, and aquatic algicide that belongs to the dicarboxylic acid chemical class. The free acid of endothall (PC Code 038901) and its dipotassium (PC Code 038904) and alkylamine (PC Code 038905) salts are registered primarily as aquatic herbicides for the control a variety of plants in water bodies. , including irrigation canals. They are also registered for desiccation/defoliation of alfalfa/clover (grown for seed only), cotton, and potatoes prior to harvest, and for reduction of sucker branch growth in hops. Permanent tolerances are established for the combined residues of endothall and its monomethyl ester at 0.1 ppm in/on cotton seeds, fish, dried hops and potatoes, and at 0.05 ppm in/on rice grain and straw [40 CFR §180.293(a)(1)].

In conjunction with a petition for tolerances on a wide variety of irrigated crops (PP# 8E7419), IR-4 has submitted a grape processing study reflecting irrigation of grapes with endothall-treated water. The chemical structure and nomenclature of endothall and its salts are listed in Table A.1. The physicochemical properties of technical grade endothall and its salts are listed in Table A.2.

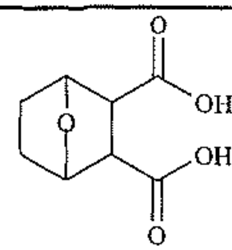
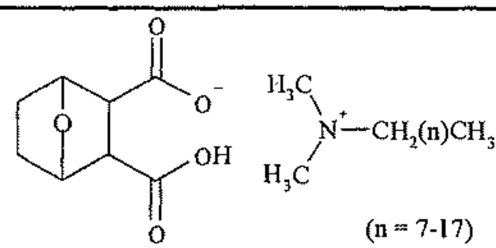
Table A.1. Endothall and Salts Nomenclature	
Chemical Structure	
Common name	Endothall
Molecular Formula	$C_8H_{10}O_5$
Molecular Weight	186.16
IUPAC name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid
CAS name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid
CAS #	145-73-3
PC Code	038901
Current Food/Feed Site Registration	Cotton, hops, potato, alfalfa grown for seed
Chemical Structure	
Common name	Endothall, mono-N,N-dimethylalkyl amine salt
Molecular Formula	Not available
Molecular Weight	Average: 422
IUPAC name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid, compound with N,N-dimethylcocoamine
CAS name	Not available
CAS #	66330-88-9
PC Code	038905
Current Food/Feed Site Registration	Cotton, hops, potato, alfalfa grown for seed, aquatic uses

Table A.2. Physicochemical Properties of Endothall and Salts		
Parameter	Value	Reference
Endothall (acid)		
Melting point	108-110℃	D187593, D187590, and D187588, 5/5/93, K. Dockter
pH	2.7 at 25℃ (1% solution)	D187593, D187590, and D187588, 5/5/93, K. Dockter
Density, bulk density, or specific gravity	0.481 g/cm^3 (bulk) at 25℃	D187593, D187590, and D187588, 5/5/93, K. Dockter
Water solubility at 25℃	109.8 g/L 13.1 g/100 mL in water, pH 5 12.7 g/100 mL in water, pH 7 12.5 g/100 mL in water, pH 9	D166798, 7/2/92, K. Dockter D207011, 9/30/94, F. Toghrol
Solvent solubility at 25℃	3.4 g/100 mL in acetonitrile 2.4 g/100 mL in n-octanol 16.0 g/100 mL in tetrahydrofuran	D207011, 9/30/94, F. Toghrol
Vapor pressure	3.92 x 10^{-5} mm Hg at 24.3℃	D166798, 7/2/92, K. Dockter
Dissociation constant, pK$_a$	4.32 for Step 1 and 6.22 for Step 2 at 20℃ (0.2% solution in 20% basic ethanol); dissociation rate 1.8-2.3 x 10^3 μmho within 3-5 minutes at □25℃, by conductivity meter	D188708, 5/3/93, K. Dockter
Octanol/water partition coefficient	Not applicable to endothall acid	D166798, 7/2/92, K. Dockter
UV/visible absorption spectrum	Not available	
Endothall, mono-N,N-dimethylalkyl amine salt		
Boiling point	Not available	
pH	5.2 at 25℃ (1% solution)	D187593, D187590, and D187588, 5/5/93, K. Dockter
Density, bulk density, or specific gravity	1.028 g/mL at 25℃	D187593, D187590, and D187588, 5/5/93, K. Dockter
Water solubility at 25℃	≥49.2 g/100mL in water, pH 5 ≥51.6 g/100 mL in water, pH 7 ≥49.8 g/100 mL in water, pH 9	D210814, 8/9/95, S. Knizner
Solvent solubility at 25℃	≥102.5 g/100mL in acetonitrile ≥95.4 g/100 mL in n-octanol ≥104.3 g/100 mL in tetrahydrofuran	D210814, 8/9/95, S. Knizner
Vapor pressure	2.09 x 10^{-5} mm Hg at 25℃ (calculated; mixed mono- and dialkylamine (C8-C20))	D206344, 9/22/94, F. Toghrol
Dissociation constant, pK$_a$	4.24 for Step 1 and 6.07 for Step 2 at 20℃ for mixed mono- and dialkylamine (C8-C20) in acidified ethanol/water; dissociation complete □17 minutes (1.7 x 10^3 μmho) at 25℃	D198885, 4/7/94, F. Toghrol
Octanol/water partition coefficient	K_{OW} 2.097 at concentrations of 8.9 x 10^{-3} M and 8.9 x 10^{-4} M, at 25℃	D209995, 1/20/95, L. Edwards
UV/visible absorption spectrum	Not available	

B. EXPERIMENTAL DESIGN

B.1. Application and Crop Information

In a field trial conducted in NY during 2006, grapes were irrigated six times with endothall-treated water using overhead sprinklers (Table B.1.1). The irrigation water was treated with endothall (2.0 lb ae/gal SC monoalkylamine salt) at a concentration of ~5 ppm, acid equivalent. The grapes were irrigated six times during fruit development at an RTI of 7 days. A total of ~1 acre inch of water (27,154 gal/A) was applied for each irrigation. Based on the concentration of the endothall and the amount of water applied, application rate for endothall was equivalent to 1.12 lb ae/A/application, for a total of 6.73 lb ae/A/season.

TABLE B.1.1. Study Use Pattern.							
Location (City, State; Year) Trial ID	End-Use Product	Application Information					
		Method; Timing	Concen. [1]	Volume (gal/A) [2]	Single Rate (lb ae/A) [3]	RTI [4] (days)	Total Rate (lb ae/A) [3]
North Rose, NY 2006 NYS01	2.0 lb ae/gal SC/L	Six broadcast foliar application during fruit development using overhead sprinklers.	4.98	26,998	1.12	7	6.73

1 The concentrate of endothall (in acid equivalents) in the irrigation water. No adjuvants were included in the irrigation water.
2 The target irrigation rate was 1 acre inch of water or 27,154 gal/A.
3 The equivalent field use rates were calculated by the reviewer based on the concentration of the endothall (ae), the application volume and plot size.
4 RTI = Retreatment Interval.

B.2. Sample Handling and Processing Procedures

Single bulk control and treated samples (~75 lbs) of grapes were harvested at 0 DAT, and were shipped fresh on the day of harvest to the processing facility, ACDS Research, Inc. (North Rose, NY). Samples were placed in cool storage prior to processing. Two subsamples of fresh unwashed grapes were collected prior to processing. Samples were processed into juice and raisins using simulated commercial procedures. The grapes were processed into juice on the day of harvest and into raisins within 2 days of harvest.

For juice production, unwashed fruits were crushed and destemmed in a crusher/destemmer and the wet mash was collected and pressed to produce the unfiltered juice. For raisins, samples were hand destemmed, placed on trays and dried in a dehydrator for 48 hours to a moisture range between 15-18%. The flow charts for juice processing and the material balance sheets for the treated samples are presented in Appendix I. For juice, the initial 47.5 lb sample of grapes was processed into 24 lb of unfiltered juice (51%) and 20.5 lbs of wet pomace (43%). For raisins, the initial 15 lb sample of grapes was dried down to yield 2.5 lb of raisins (17%).

The whole fruit, juice and raisin samples were transferred to frozen storage (≤-10°C) immediately after processing and shipped frozen via ACDS freezer truck 21-23 days later to United Phosphorous, Inc. (King of Prussia, PA). After homogenization, processed samples were shipped by overnight courier on dry ice to ALS Laboratory Group. At ALS, the processed samples were stored frozen (≤-10°C) prior to analysis.

B.3. Analytical Methodology

Residues of the free acid of endothall in/on grapes and grape processed fractions were determined using a LC/MS/MS method (Method No. KP-242R1) entitled "Analytical Method for Determination of Endothall in Crops", issued 5/4/2007.

For this method, residues were extracted twice by homogenization with water followed by centrifugation and filtering. Residues were then derivatized with HFTH in 50% H_3PO_4 at 100-120°C for 90 minutes. After cooling, the derivatized residues were partitioned into MTBE, evaporated to dryness, and reconstituted in hexane:MTBE (1:1 v:v). Residues were then cleaned using an amine SPE cartridge eluted with methanol:MTBE (1:4). Residues were analyzed by LC/MS/MS using external standards. The m/z 397→166 ion transition was used for quantifying residues. The validated LOQ for endothall is 0.05 ppm, and the reported LOD is 0.0001 ppm.

For method validation, control samples of grapes and raisins were fortified with endothall at 0.05-5.0 ppm.

C. RESULTS AND DISCUSSION

The LC/MS/MS method used for determining residues of endothall in/on grapes and grape processed fractions was adequately validated prior to and in conjunction with the analysis of processing study samples (Table C.1). Method validation recovery averaged 90% with a standard deviation of 13% for grapes, concurrent recoveries averaged 101% with a standard deviation of 19% for grapes and averaged 110% for raisins (n=2). Apparent residues of endothall were non-detectable in/on control samples. Adequate sample calculations and example chromatograms were provided and the fortification levels used for method recoveries were similar in magnitude to the measured residue levels.

Grape, juice and raisin samples were stored frozen at ≤-10°C for up to 379 days prior to analysis (Table C.2). Adequate storage stability data are available indicating that endothall is stable in frozen tomatoes for up to 467 days (47520719.der, under review). The stability data for tomatoes will support the storage durations and conditions for the processing study.

Residues of endothall averaged 0.280 ppm in/on whole grapes (RAC) were 1.24 ppm in juice and 1.21 ppm in raisins (Table C.3). The calculated processing factors for juice and raisins were 4.3x and 4.4x, respectively. The theoretical concentration factors are 4.7x for raisins and 1.2x for juice. Although the observed processing factor for juice is substantially higher than the theoretical value, no explanation was provided as to why residue concentrated to such an extent in juice.

TABLE C.1. Summary of Method Validation and Concurrent Recoveries of Endothall from Grapes.

Matrix	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean ± Std. Dev. (%)
Method Validation				
Fruit	0.05	3	74, 71, 76	74±3
	0.5	3	96, 102, 106	101 ± 5
	5.0	3	96, 95, 97	96 ± 1
	Total	**9**	**71-106**	**90 ± 13**
Concurrent Recoveries				
Fruit	0.05	2	95, 112	104
	5.0	2	76, 119	97
	Total	**4**	**76-119**	**101 ± 19**
Raisins	0.05	1	106	110
	5.0	1	113	

TABLE C.2. Summary of Storage Conditions.

Matrix	Storage Temperature (°C)	Actual Storage Duration (days)[1]	Interval of Demonstrated Storage Stability (days)[2]
Grape	≤-10	377-379	467
Juice			
Raisins			

[1] Interval from harvest to extraction for analysis. Extracts were stored 11-12 days prior to analysis.
[2] Endothall is stable in frozen tomatoes for up to 467 days (47520719.der under review).

TABLE C.3. Residue Data from Grape Processing Study with Endothall.

RAC	Processed Commodity	Total Rate [1]	PHI (days)	Residues (ppm) [2]	Processing Factor
Grape	Unwashed whole fruit (RAC)	5 ppm	0	0.291, 0.269 (ave. 0.280)	--
	Juice	(6.73 lb ae/A)		1.21	4.3x
	Raisin			1.24	4.4x

[1] The rate is expressed both in terms of the concentration in the irrigation water (ppm) and the total amount (lb ae/A) applied.
[2] Residues are expressed in acid equivalents. The LOQ is 0.05 ppm.

D. CONCLUSION

The grape processing study is adequate and indicates that endothall residues can concentrate in raisins (4.4x). It does not provide acceptable information about juice processing.

E. REFERENCES

None.

F. DOCUMENT TRACKING

RDI: David Soderberg (5 June 2009); William Donovan (5 June 2009)
Petition Number: 8E7419
DP#: 356315
PC Code: 038901, 038905

Template Version June 2005

Appendix I. Grape Juice Processing Flow Chart and Mass Balance Sheets for Juice and Raisin Processing (Treated Samples).

Interregional Research Project No. 4 **PR. No. Z9754** **Page 101**

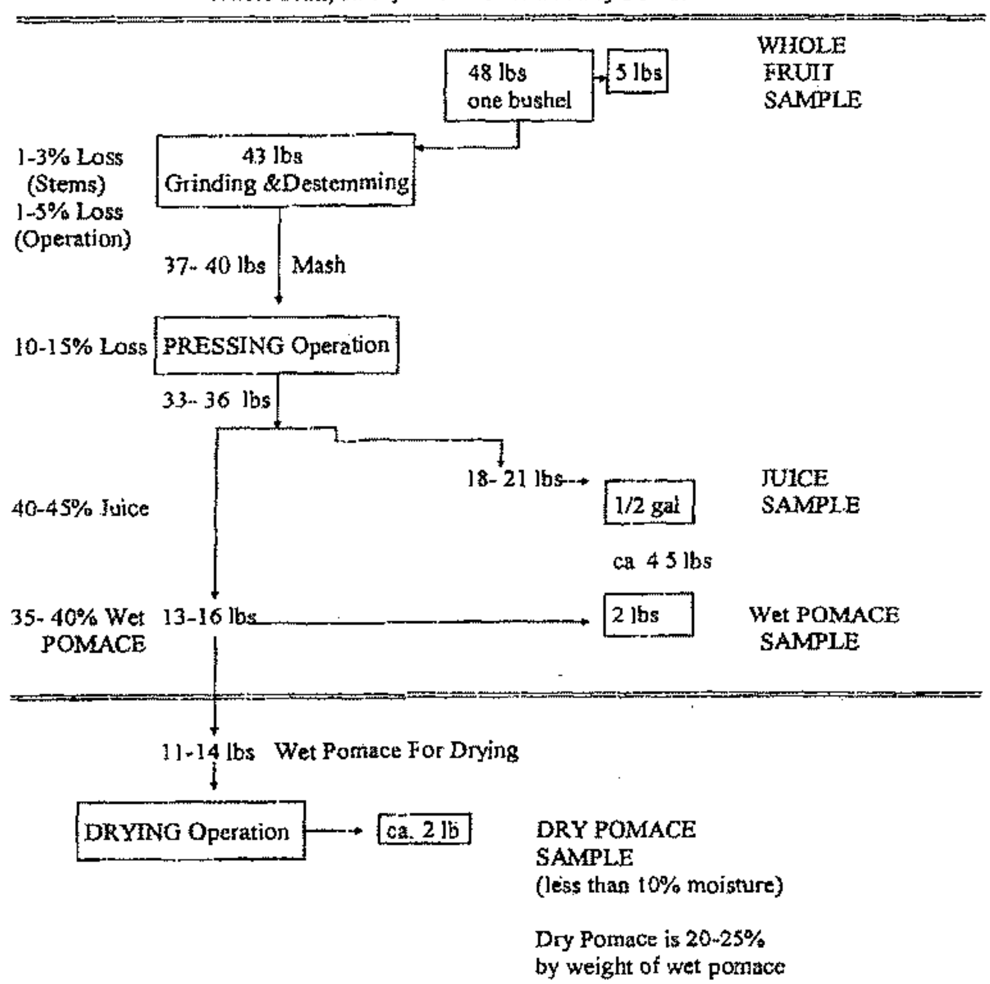
Z9754.06-AC002

A C D S Research, Inc

FLOW CHART

Typical Small Batch Grape Processing Simulating Commercial Processing

~~Whole Fruit, Juice, Wet Pomace and Dry Pomace Fractions~~



A C D S. Research, Inc.

FRUIT PROCESSING CALCULATION WORKSHEET (GRAPES)

Sponsor Trial No: Z9754.06-AC002 ACDS Processing No: AR06908

F - Sample No 2 - Treatment No., ___ Untreated, X Treated

STEP 1: (Initial Sample Size)

75.0 - Gross Weight (lbs) of sample (Fruit + Containers) 1 - No. of Containers.

- 25.0 - Tare Weight (lbs - weight of containers) - 3.5 lb + 21.5 lb Grapes for Raisins

= 50.0 - Net Weight (lbs) of fruit for processing (Transcribe to "Net Weight" column for "Starting Weight" and "Whole Fruit Washed" or "Whole Fruit Unwashed" on the ACDS Fruit Processing Form)

- 2.5 - Weight (lbs) of Whole Fruit Sample (Transcribe to "Sample Weight" column for "Whole Fruit Washed" or "Whole Fruit Unwashed").

= 47.5 - Fruit (lbs) for destemmer

STEP 2: (Wet Mash)

57.0 - Gross Weight (lbs) of Wet Mash produced (Wet Mash + Tub)

- 13.5 - Tare Weight (lbs - weight of tub).

= 43.5 - Net Weight (lbs) of Wet Mash for pressing (Transcribe to "Net Weight" column for "Total Amount Of Wet Mash Produced").

STEP 3: (Juice)

26.0 - Gross Weight (lbs) of Juice produced (Juice + Pail w/ Liner)

- 2.0 ~~24.0~~ - Tare Weight (lbs - pail w/ liner: 1 No. Pails x 2 lbs/Pail) GXJ 10/4/06 Entry Error

= 24.0 - Net Weight (lbs) of Juice produced (Transcribe to "Net Weight" column for Juice).

- 5.0 - Weight (lbs) of Juice Sample (Transcribe to "sample Weight" column for Juice)

STEP 4: (Wet Pomace)

22.5 - Gross Weight (lbs) of Wet Pomace produced (Wet Pomace + Pail w/ Liner)

- 2.0 - Tare Weight (lbs - pail w/ liner: 1 No. Pails x 2 lbs/Pail)

= 20.5 - Net Weight of Pomace produced (Transcribe to "Net Weight" column for Wet Pomace)

- -0- - Weight (lbs) of Wet Pomace sample (Transcribe to "Sample Weight" column for Wet Pomace).

Signature: Grant L Jordan Date: 10 / 4 / 06

A C D S Research, Inc SOP/R/03/R7

A C D S Research, Inc

FRUIT PROCESSING FORM (GRAPES)

Date: 10 / 4 / 06 Sponsor Trial No : Z9754.06-ACD02 ACDS Processing No : AR06408

Preprocessing Equipment Cleaning:
X All equipment cleaned with soap and water before use
___ Other:

Treatment No 2, Control ___, Treated X

Requested Fraction Amounts (lbs):
Whole Fruit X Juice X Wet Pomace ___ Dry Pomace ___
Other

Processing (Grinding, Pressing, Juice, Wet Pomace, and Dry Pomace [if necessary] Collection Note – weights transcribed from attached Fruit Processing Calculation Worksheet):

FRACTIONS	Net Weight (Lbs.)	Sample ID	Sample Wt. (Lbs.)	Time Cooled	Time Frozen
Starting Weight	50.0				
Whole Fruit Washed					
Whole Fruit Unwashed	2.5	N	2.5	5:15 PM	6:30 PM
Total Amount of Wet Mash Produced	43.5				
Juice	24.0	P	5.0	6:20 PM	6:30 PM
Wet Pomace	20.5				
Wet Pomace Used In Drying					
Dry Pomace		GZJ 10/4/06			

Drying Date: __/__/__ Start ___ AM/PM Finish ___ AM/PM
Drying Temperature Range: ___ deg. F to ___ deg F.
___ Lb Wet Pomace Used- ___ Lb Dry Pomace = ___ Wt. Loss (Lbs.)

50.0 Starting Weight - 47.0 Fruit Fractions (Whole Fruit Sample Weight + Net Weight of Juice, Wet Pomace, and Dry Pomace [if necessary]) = 3.0 Processing Loss (Lbs.).

Signature: Grant Z Jordan Date: 10 / 4 / 06

ACDS Research, Inc

FRUIT PROCESSING FORM (Raisin Grapes)

Date: 10 / 6 / 06 Sponsor Trial No: 29754.06-AQ002 ACDS Processing No: AR0640B

Preprocessing Equipment Cleaning:
X All equipment cleaned with soap and water before use
Other:

Treatment No. 2, Control ____, Treated X

Requested Fraction Amounts (lbs):
Whole Fruit X Raisins X Other

Processing (Destemming and Drying):

FRACTIONS	Net Weight (Lbs.)	Sample ID	Sample Wt. (Lbs.)	Time Cooled	Time Frozen
Starting Weight	21.5				
Whole Fruit Washed					
Whole Fruit Unwashed	2.5	1	2.5	10/4/06 625	6:30 PM
Total Amount Used For Drying					
Raisins	2.5	2	2.5	10/6/06	5:30 PM
Other:					

Drying: Date/Time Start 10 / 4 / 06 5:40 AM/PM, Date/Time Finish 10 / 6 / 06 5:15 AM/PM
Drying Temperature Range: 130 deg. F to 140 deg. F.
15.0 Lb Grapes Used - 2.5 Lb Raisins = 12.5 Wt. Loss (Lbs)

21.5 Starting Weight - 5.0 Fruit Fractions (Whole Fruit Sample Weight + Net Weight of Raisins and Other) = 16.5 Processing Loss (Lbs)

Signature: Grant L Jordan Date: 10 / 6 / 06

Primary Evaluator	David Soderberg, Chemist, RABV, HED	Date: 5 June 2009
Approved by	William Donovan, Senior Scientist, RABV, HED	Date: 5 June 2009

This DER was originally prepared under contract by Dynamac Corporation (1910 Sedwick Road, Building 100, Suite B, Durham, NC 27713; submitted 3/27/2009). The DER has been reviewed by the Health Effects Division (HED) and revised as needed for clarity, correctness and to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORT:

47520717. Arsenovic, M. (2008) Endothall (Hydrothol 191): Magnitude of the Residue on Mint: Lab Project Number: Z9758, Z9758.07-CER13 Unpublished study prepared by Interregional Research Project No. 4. 253 pages.

EXECUTIVE SUMMARY:

Interregional Research Project No. 4 (IR-4) submitted field trial data reflecting the exposure of mint to endothall through the use of treated irrigation water. In two mint field trials conducted during 2006 and 2007 in Zones 5 and 11, a 2.0 lb ae/gal soluble concentrate (SC/L) formulation of endothall (monoalkylamine salt) was used to treat the irrigation water at a rate of 5 ppm ae. [In order to avoid the complications of different molecular weights for different salts, endothall concentrations are expressed as the free acid equivalents (ae).] The treated water was applied to the mint during vegetative development as six broadcast foliar applications using overhead sprinklers, at retreatment intervals (RTIs) of 6-7 days. A volume equivalent to ~1 acre inch of water (27,154 gal/A) was applied for each application. Based on the concentration of the endothall and the amount of water applied, the application rates for endothall were equivalent to 1.11-1.13 lb ae/A/application, for a total of 6.64-6.77 lb ae/A/season.

Single control and duplicate treated samples of mint tops were harvested from each test on the day of the final application (0 days after treatment, DAT), and samples were stored at ≤-18°C for up to 336 days prior to analysis. Adequate storage stability data are available to support the duration and conditions of sample storage.

Residues of endothall (free acid) in/on mint tops were determined using an adequate LC/MS/MS method (Method No. KP-242R1). For this method, residues were extracted with water and then derivatized with heptafluoro-*p*-tolylhydrazine (HFTH) in 50% H_3PO_4. The derivatized residues were cleaned up by partitioning into methyl t-butyl ether (MTBE) and elution through an amine solid phase extraction (SPE) cartridge. Residues were then analyzed by LC/MS/MS using external standards for quantitation. Residues are expressed in endothall acid equivalents. The validated limit of quantitation (LOQ) for endothall in/on mint is 0.05 ppm.

Following six overhead sprinkler applications with irrigation water containing endothall at 5 ppm (6.74-6.77 lb ae/A/season), endothall residues were 1.31-2.89 ppm in/on four samples of mint harvested at 0 DAT. Average endothall residues were 2.14 ppm, and the highest average field trial (HAFT) residues were 2.80 ppm. No residue decline data was provided.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the mint field trial residue data are classified as scientifically acceptable. Although limited field trials were performed, these applications are expected to be conservative relative to actual inadvertent applications. The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document, DP# 356315.

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported which would have an adverse impact on the validity of the study.

A. BACKGROUND INFORMATION

Endothall [7-oxabicyclo[2,2,1] heptane-2,3-dicarboxylic acid] is a selective contact herbicide, defoliant, desiccant, and aquatic algaecide that belongs to the dicarboxylic acid chemical class. The free acid of endothall (PC Code 038901) and its dipotassium (PC Code 038904) and amine (PC Code 038905) salts are registered primarily as aquatic herbicides for the control a variety of plants in water bodies, including irrigation canals. They are also registered for desiccation/ defoliation of alfalfa/clover (grown for seed only), cotton, and potatoes prior to harvest, and for reduction of sucker branch growth in hops. Permanent tolerances are established for the combined residues of endothall and its monomethyl ester at 0.1 ppm in/on cotton seeds, fish, dried hops and potatoes, and at 0.05 ppm in/on rice grain and straw [40 CFR §180.293(a)(1)].

In conjunction with a petition for tolerances on a wide variety of irrigated crops (PP# 8E7419), IR-4 has submitted field trial data reflecting irrigation of mint with endothall-treated water. The chemical structure and nomenclature of endothall and its monoalkylamine salt are listed in Table A.1. The physicochemical properties of technical grade endothall and its monoalkylamine salt are listed in Table A.2.

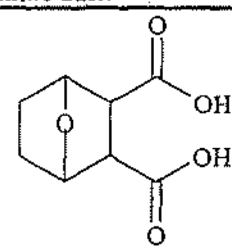
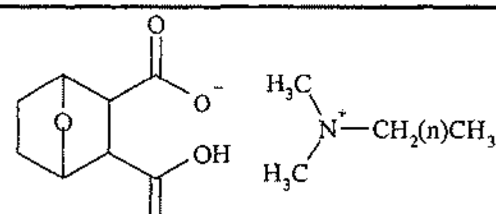
Table A.1. Nomenclature of Endothall and its Monoalkylamine Salt.	
Chemical Structure	
Common name	Endothall
Molecular Formula	$C_8H_{10}O_5$
Molecular Weight	186.16
IUPAC name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid
CAS name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid
CAS #	145-73-3
PC Code	038901
Current Food/Feed Site Registration	Cotton, hops, potato, alfalfa grown for seed
Chemical Structure	 (n = 7-17)
Common name	Endothall, mono-N,N-dimethylalkyl amine salt
Molecular Formula	Not available
Molecular Weight	Average: 422
IUPAC name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid, compound with N,N-dimethylcocoamine
CAS name	Not available
CAS #	66330-88-9
PC Code	038905
Current Food/Feed Site Registration	Cotton, hops, potato, alfalfa grown for seed, aquatic uses

Table A.2. Physicochemical Properties of Endothall and Its Monoalkylamine Salt.		
Parameter	Value	Reference
Endothall (acid)		
Melting point	108-110℃	D187593, D187590, and D187588, 5/5/93, K. Dockter
pH	2.7 at 25℃ (1% solution)	D187593, D187590, and D187588, 5/5/93, K. Dockter
Density, bulk density, or specific gravity	0.481 g/cm^3 (bulk) at 25℃	D187593, D187590, and D187588, 5/5/93, K. Dockter
Water solubility at 25℃	109.8 g/L 13.1 g/100 mL in water, pH 5 12.7 g/100 mL in water, pH 7 12.5 g/100 mL in water, pH 9	D166798, 7/2/92, K. Dockter D207011, 9/30/94, F. Toghrol
Solvent solubility at 25℃	3.4 g/100 mL in acetonitrile 2.4 g/100 mL in n-octanol 16.0 g/100 mL in tetrahydrofuran	D207011, 9/30/94, F. Toghrol
Vapor pressure	3.92 x 10^{-5} mm Hg at 24.3℃	D166798, 7/2/92, K. Dockter

Table A.2. Physicochemical Properties of Endothall and Its Monoalkylamine Salt.

Parameter	Value	Reference
Dissociation constant, pK_a	4.32 for Step 1 and 6.22 for Step 2 at 20℃ (0.2% solution in 20% basic ethanol); dissociation rate 1.8-2.3 x 10^3 µmho within 3-5 minutes at □25℃, by conductivity meter	D188708, 5/3/93, K. Dockter
Octanol/water partition coefficient	Not applicable to endothall acid	D166798, 7/2/92, K. Dockter
UV/visible absorption spectrum	Not available	
Endothall, mono-N,N-dimethylalkyl amine salt		
Boiling point	Not available	
pH	5.2 at 25℃ (1% solution)	D187593, D187590, and D187588, 5/5/93, K. Dockter
Density, bulk density, or specific gravity	1.028 g/mL at 25℃	D187593, D187590, and D187588, 5/5/93, K. Dockter
Water solubility at 25℃	≥49.2 g/100mL in water, pH 5 ≥51.6 g/100 mL in water, pH 7 ≥49.8 g/100 mL in water, pH 9	D210814, 8/9/95, S. Knizner
Solvent solubility at 25℃	≥102.5 g/100mL in acetonitrile ≥95.4 g/100 mL in n-octanol ≥104.3 g/100 mL in tetrahydrofuran	D210814, 8/9/95, S. Knizner
Vapor pressure	2.09 x 10^{-5} mm Hg at 25℃ (calculated; mixed mono- and dialkylamine (C8-C20))	D206344, 9/22/94, F. Toghrol
Dissociation constant, pK_a	4.24 for Step 1 and 6.07 for Step 2 at 20℃ for mixed mono- and dialkylamine (C8-C20) in acidified ethanol/water; dissociation complete □17 minutes (1.7 x 10^3 µmho) at 25℃	D198885, 4/7/94, F. Toghrol
Octanol/water partition coefficient	K_{OW} 2.097 at concentrations of 8.9 x 10^{-3} M and 8.9 x 10^{-4} M, at 25℃	D209995, 1/20/95, L. Edwards
UV/visible absorption spectrum	Not available	

B. EXPERIMENTAL DESIGN

B.1. Study Site Information

Two mint field trials were conducted in Zones 5 and 11 during 2006 and 2007 (Table B.1.1). The irrigation water used in each test was treated with endothall (2.0 lb ae/gal SC monoalkylamine salt) at a concentration of ~5 ppm, acid equivalent. The treated water was applied to the mint during vegetative development as six broadcast foliar applications using overhead sprinklers, at RTIs of 6-7 days. A volume equivalent to ~1 acre inch of water (~27,154 gal/A) was applied for each application. Based on the concentration of the endothall and the amount of water applied, application rates for endothall were equivalent to 1.11-1.13 lb ae/A/application, for a total of 6.64-6.77 lb ae/A/season (Table B.1.3). These applications are expected to be conservative relative to actual applications.

TABLE B.1.1. Trial Site Conditions.

Trial Identification (City, State; Year)	Soil characteristics[1]			
	Type	%OM	pH	CEC (meq/100g)
Ephrata, WA 2006 WA$09	Loamy Sand	1.0	7.4	12.4
Elkhorn, WI 2007 WI$39	Muck	>70%	NR	NR

[1]These parameters are optional except in cases where their value affects the use pattern for the chemical.

TABLE B.1.2. Water Characterization.					
Study site	Water characteristics				
	Type	Hardness/Salinity	pH	Turbidity	Dissolved OM
Ephrata, WA 2006 WA$09	Well	NR	NR	NR	NR
Elkhorn, WI 2007 WI$39	Well	NR	NR	NR	NR

NR = Not reported.

The actual temperature recordings and rainfall were typical for each site and no unusual weather conditions were reported. No additional irrigation was reported during the study period. The tests were conducted according to normal agricultural practices for the regions, and information was provided on maintenance pesticides and fertilizers used at each site. No information was provided on the characteristics of the water used for irrigation, other than the source (Table B.1.2).

TABLE B.1.3. Study Use Pattern.							
Location (City, State; Year) Trial ID	End-Use Product	Application Information					
		Method; Timing	Concen. [1]	Volume (gal/A) [2]	Single Rate (lb ae/A) [3]	RTI [4] (days)	Total Rate [4] (lb ae/A)
Ephrata, WA 2006 WA$09	2.0 lb/gal SC	Six broadcast foliar application during vegetative development using overhead sprinklers.	4.97-5.00	26,715	1.11	7	6.64
Elkhorn, WI 2007 WI$39	2.0 lb/gal SC	Six broadcast foliar application during vegetative development using overhead sprinklers.	27,140	5.00	1.13	6-7	6.77

[1] The concentration of endothall (in acid equivalents) in the irrigation water. No adjuvants were included in the irrigation water.
[2] The target irrigation rate was 1 acre inch of water or 27,154 gal/A.
[3] The equivalent field use rates were calculated by the reviewer based on the concentration of the endothall (ae), the application volume and plot size.
[4] RTI = Retreatment Interval.

TABLE B.1.3. Trial Numbers and Geographical Locations.

NAFTA Growing Zones[2]	Mint		
	Submitted	Requested[1]	
		Canada	U.S.
1	--	--	--
2	--	--	--
3	--	--	--
4	--	--	--
5	1	--	2
6	--	--	--
7	--	--	--
8	--	--	--
9	--	--	--
10	--	--	--
11	1	--	3
12	--	--	--
13	--	--	--
Total	2	--	5

[1] Based on EPA OPPTS Guideline 860.1500.
[2] Zones 1A, 5 A and B, 7A and 14-21 were not included as the proposed use is for the U.S. only.

B.2. Sample Handling and Preparation

Duplicate control and treated samples (≥4 lbs/sample) of mint tops were harvested at 0 DAT (after the sixth application) and placed in frozen storage at the test facilities within 45 minutes. Samples were stored frozen at the field sites for 15-34 days prior to shipment by ACDS Freezer truck to the analytical laboratory, Cerexagri, Inc. (King of Prussia, PA), where samples were store at ≤-18°C until analysis.

B.3. Analytical Methodology

Residues of endothall (free acid) in/on mint tops were determined using a LC/MS/MS method (Method No. KP-242R1) entitled "Analytical Method for Determination of Endothall in Crops", issued 5/4/2007.

For this method, residues were extracted twice by homogenization with water followed by centrifugation and filtering. Residues were then derivatized with HFTH in 50% H_3PO_4 at 100-120°C for 90 minutes. After cooling, the derivatized residues were partitioned into MTBE, evaporated to dryness, and reconstituted in hexane:MTBE (1:1 v:v). Residues were then cleaned using an amine SPE cartridge eluted with methanol:MTBE (1:4). Residues were analyzed by LC/MS/MS using external standards. The m/z 397→166 ion transition was used for quantifying residues. Residues are expressed in endothall acid equivalents. The validated LOQ for endothall in/on mint is 0.05 ppm. An LOD of 0.0001 ppm was reported; however, this value was the instrument LOD, rather than the LOD of residue in a control matrix.

The above method was validated prior to and in conjunction with the analysis of the field trial samples. Control samples of mint were fortified with endothall at 0.05-5.0 ppm for method validation and at 0.05-4.0 ppm for concurrent recoveries.

C. RESULTS AND DISCUSSION

The LC/MS/MS method used for determining residues of endothall in/on mint was adequately validated prior to and in conjunction with the analysis of field trial samples. Method validation recovery averaged 78% with a standard deviation of 8%, and concurrent recoveries averaged 79% with a standard deviation of 6% (Table C.1). Apparent residues of endothall were <LOQ in/on control samples. Adequate sample calculations and example chromatograms were provided and the fortification levels used for method recoveries were similar in magnitude to the measured residue levels.

Mint top samples were stored frozen at ≤-18°C for up to 336 days prior to analysis (Table C.2). Adequate storage stability data are available indicating that endothall is stable in frozen lettuce for up to 469 days (47520719.der, under review). The stability data for lettuce will support the storage durations and conditions for the current mint field trials.

Following six overhead sprinkler applications with irrigation water containing endothall at 5 ppm (6.64-6.77 lb ae/A/season), endothall residues were 1.31-2.89 ppm in/on four mint samples harvested at 0 DAT (Table C.3). Average endothall residues were 2.14 ppm, and the HAFT residues were 2.80 ppm (Table C.4). No residue decline data was provided.

Common cultural practices were used to maintain plants, and the weather conditions and maintenance chemicals and fertilizer used in this study did not have a notable impact on the residue data. Phytotoxicity was noted at the WA test site. At this site, the treated plot showed reduced development and regrowth, resulting in a stunted less vigorous crop. Although the apparent phytotoxicity resulted in less biomass, adequate sample material was available for representative duplicate treated samples.

TABLE C.1. Summary of Method Validation and Concurrent Recoveries of Endothall from Mint.

Matrix	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean ± Std. Dev. (%)
Method Validation				
Tops	0.05	3	74, 72, 71	72 ± 2
	0.5	3	72, 72, 74	73 ± 2
	5.0	3	85, 90, 90	88 ± 3
	Total	9	71-90	78 ± 8
Concurrent Recoveries				
Tops	0.05	2	85, 78	82
	2	1	72	72
	4	1	82	82
	Total	4	72-85	79 ± 6

[1] Standard deviations are calculated for data sets having ≥3 values.

TABLE C.2. Summary of Storage Conditions.

Matrix	Storage Temperature (°C)	Actual Storage Duration (days)[1]	Interval of Demonstrated Storage Stability (days)[2]
Mint tops	≤-18	22-336	469

[1] Interval from harvest to extraction for analysis. Samples were extracted the day of analysis.
[2] Endothall is stable in frozen lettuce for up to 469 days (47520719.der under review).

TABLE C.3. Residue Data from Mint Field Trials with Endothall Monoalkylamine Salt (SC/L).

Trial ID (City, State; Year)	Zone	Crop/Variety	Matrix	Total Rate[1]		PHI (days)	Residues (ppm)[2,3]	
				ppm	lb ae/A			
Ephrata, WA 2006 WA$09	11	Mint (Todd's Mitchem)	Tops	5.0	6.64	0	2.89	2.70
Elkhorn, WI 2007 WI$39	5	Mint (Black Mitchem)	Tops	5.0	6.77	0	1.67	1.31

[1] The rate is expressed both in terms of the concentration in the irrigation water (ppm) and the total amount (lb ae/A) applied.
[2] Expressed in acid equivalents. The LOQ is 0.05 ppm.
[3] The two results for each field trial represent two samples taken from a single plot, not two plots.

TABLE C.4. Summary of Residue Data from Mint Field Trials with Endothall Monoamine Salt (SC/L).

Commodity	Total Applic. Rate[1]	PHI (days)	Residue Levels (ppm)[2]						
			n	Min.	Max.	HAFT[3]	Median (STMdR)	Mean (STMR)	Std. Dev.
Mint	5 ppm (6.64-6.77)	0	2	1.49	2.80	2.80	2.14	2.14	0.923

[1] The value in parentheses is the total application rate in terms of lb ae/A.
[2] Residues are expressed in terms of the free acid. The LOQ is 0.05 ppm.
[3] HAFT = Highest Average Field Trial.

D. CONCLUSION

The available field trial data are adequate and support the use of endothall-treated water for irrigation of mint. The data support the use of endothall in irrigation water at a concentration of 5 ppm ae, with no more that six applications per season and a minimum 7-day interval between applications to the water. Residues on the mint were determined at a 0-day PHI.

E. REFERENCES

None

F. DOCUMENT TRACKING

RDI: David Soderberg (5 June 2009); William Donovan (5 June 2009);
Petition Number: 8E7419
DP#: 356315
PC Code: 038901 and 038905

Template Version June 2005

Primary Evaluator	David Soderberg, Chemist, RABV, HED	Date: 5 June 2009
Approved by	William Donovan, Senior Scientist, RABV, HED	Date: 5 June 2009

This DER was originally prepared under contract by Dynamac Corporation (1910 Sedwick Road, Building 100, Suite B, Durham, NC 27713; submitted 3/27/2009). The DER has been reviewed by the Health Effects Division (HED) and revised as needed for clarity, correctness and to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORT:

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EXECUTIVE SUMMARY:

Interregional Research Project No. 4 (IR-4) submitted a mint processing study reflecting the exposure of mint to endothall through the use of treated irrigation water. In a field trial conducted in WA (Zone 11) during 2006, a 2.0 lb ae/gal soluble concentrate (SC/L) formulation of endothall (monoalkylamine salt) was used to treat the irrigation water at a rate of 5 ppm ae. [In order to avoid the complications of different molecular weights for different salts, endothall concentrations are expressed as the free acid equivalents (ae).] The treated water was then applied using overhead sprinklers to mint as six broadcast foliar applications during vegetative development at retreatment intervals (RTIs) of 7 days. A volume equivalent to 1 acre inch of water (~27,154 gal/A) was applied for each application. Based on the concentration of the endothall in the irrigation water and the amount of water applied, the application rate for endothall was equivalent to 1.11 lb ae/A/application, for a total of 6.64 lb ae/A/season.

Single bulk control and treated samples of mint tops were harvested at normal crop maturity, immediately following the last irrigation (0 days after treatment, DAT). The tops were processed into oil using simulated commercial procedures. Samples of tops and oil were stored at ≤-17°C for up to 366 and 241 days, respectively, prior to analysis. The sample storage intervals and conditions are supported by the available storage stability data.

Residues of endothall (free acid) in/on mint tops and oil were determined using an adequate LC/MS/MS method (Method No. KP-242R1). Residues in tops were extracted with water and then derivatized with heptafluoro-*p*-tolylhydrazine (HFTH) in 50% H_3PO_4. Oil samples were diluted with water and partitioned against hexane, and the aqueous soluble residues were then derivatized with HFTH. The derivatized residues from each matrix were then cleaned up by partitioning into methyl t-butyl ether (MTBE) followed by elution through an amine solid phase extraction (SPE) cartridge. Residues were then analyzed by LC/MS/MS using external standards for quantitation. The validated limit of quantitation (LOQ) for endothall is 0.05 ppm in each mint matrix, and the estimated limit of detection (LOD) was reported to be 0.0001 ppm.

Following six overhead sprinkler applications of endothall (monoalkylamine salt) to mint at rates totaling 6.64 lb ae/A, residues were 3.96 ppm in mint tops (RAC) and nondetectable (<0.0001 ppm) in mint oil, indicating that the processing factor of endothall in mint oil is <0.001x.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the mint processing residue data are scientifically acceptable. The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document, DP# 356315.

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported which would have an adverse impact on the validity of the study.

A. BACKGROUND INFORMATION

Endothall [7-oxabicyclo[2,2,1] heptane-2,3-dicarboxylic acid] is a selective contact herbicide, defoliant, desiccant, and aquatic algaecide that belongs to the dicarboxylic acid chemical class. The free acid of endothall (PC Code 038901) and its dipotassium (PC Code 038904) and alkylamine (PC Code 038905) salts are registered primarily as aquatic herbicides for the control a variety of plants in water bodies. , including irrigation canals. They are also registered for desiccation/ defoliation of alfalfa/clover (grown for seed only), cotton, and potatoes prior to harvest, and for reduction of sucker branch growth in hops. Permanent tolerances are established for the combined residues of endothall and its monomethyl ester at 0.1 ppm in/on cotton seeds, fish, dried hops and potatoes, and at 0.05 ppm in/on rice grain and straw [40 CFR §180.293(a)(1)].

In conjunction with a petition for tolerances on a wide variety of irrigated crops (PP# 8E7419), IR-4 has submitted field trial data reflecting irrigation of mint with endothall-treated water. The chemical structure and nomenclature of endothall and its monoalkylamine salt are listed in Table A.1. The physicochemical properties of technical grade endothall and its monoalkylamine salt are listed in Table A.2.

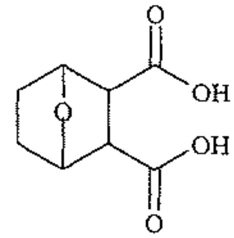
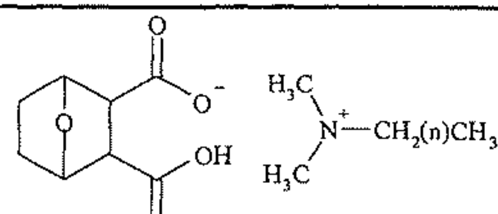
Table A.1. Nomenclature of Endothall and its Monoalkylamine Salt.	
Chemical Structure	
Common name	Endothall
Molecular Formula	$C_8H_{10}O_5$
Molecular Weight	186.16
IUPAC name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid
CAS name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid
CAS #	145-73-3
PC Code	038901
Current Food/Feed Site Registration	Cotton, hops, potato, alfalfa grown for seed
Chemical Structure	 (n = 7-17)
Common name	Endothall, mono-N,N-dimethylalkyl amine salt
Molecular Formula	Not available
Molecular Weight	Average: 422
IUPAC name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid, compound with N,N-dimethylcocoamine
CAS name	Not available
CAS #	66330-88-9
PC Code	038905
Current Food/Feed Site Registration	Cotton, hops, potato, alfalfa grown for seed, aquatic uses

Table A.2. Physicochemical Properties of Endothall and Its Monoalkylamine Salt.		
Parameter	Value	Reference
Endothall (acid)		
Melting point	108-110°C	D187593, D187590, and D187588, 5/5/93, K. Dockter
pH	2.7 at 25°C (1% solution)	D187593, D187590, and D187588, 5/5/93, K. Dockter
Density, bulk density, or specific gravity	0.481 g/cm^3 (bulk) at 25°C	D187593, D187590, and D187588, 5/5/93, K. Dockter
Water solubility at 25°C	109.8 g/L 13.1 g/100 mL in water, pH 5 12.7 g/100 mL in water, pH 7 12.5 g/100 mL in water, pH 9	D166798, 7/2/92, K. Dockter D207011, 9/30/94, F. Toghrol
Solvent solubility at 25°C	3.4 g/100 mL in acetonitrile 2.4 g/100 mL in n-octanol 16.0 g/100 mL in tetrahydrofuran	D207011, 9/30/94, F. Toghrol
Vapor pressure	3.92 x 10^{-5} mm Hg at 24.3°C	D166798, 7/2/92, K. Dockter

Table A.2. Physicochemical Properties of Endothall and Its Monoalkylamine Salt.		
Parameter	Value	Reference
Dissociation constant, pK_a	4.32 for Step 1 and 6.22 for Step 2 at 20°C (0.2% solution in 20% basic ethanol); dissociation rate 1.8-2.3 x 10^3 µmho within 3-5 minutes at □25°C, by conductivity meter	D188708, 5/3/93, K. Dockter
Octanol/water partition coefficient	Not applicable to endothall acid	D166798, 7/2/92, K. Dockter
UV/visible absorption spectrum	Not available	
Endothall, mono-N,N-dimethylalkyl amine salt		
Boiling point	Not available	
pH	5.2 at 25°C (1% solution)	D187593, D187590, and D187588, 5/5/93, K. Dockter
Density, bulk density, or specific gravity	1.028 g/mL at 25°C	D187593, D187590, and D187588, 5/5/93, K. Dockter
Water solubility at 25°C	≥49.2 g/100mL in water, pH 5 ≥51.6 g/100 mL in water, pH 7 ≥49.8 g/100 mL in water, pH 9	D210814, 8/9/95, S. Knizner
Solvent solubility at 25°C	≥102.5 g/100mL in acetonitrile ≥95.4 g/100 mL in n-octanol ≥104.3 g/100 mL in tetrahydrofuran	D210814, 8/9/95, S. Knizner
Vapor pressure	2.09 x 10^{-5} mm Hg at 25°C (calculated; mixed mono- and dialkylamine (C8-C20))	D206344, 9/22/94, F. Toghrol
Dissociation constant, pK_a	4.24 for Step 1 and 6.07 for Step 2 at 20°C for mixed mono- and dialkylamine (C8-C20) in acidified ethanol/water; dissociation complete □17 minutes (1.7 x 10^3 µmho) at 25°C	D198885, 4/7/94, F. Toghrol
Octanol/water partition coefficient	K_{OW} 2.097 at concentrations of 8.9 x 10^{-3} M and 8.9 x 10^{-4} M, at 25°C	D209995, 1/20/95, L. Edwards
UV/visible absorption spectrum	Not available	

B. EXPERIMENTAL DESIGN

B.1. Application and Crop Information

In a field trial conducted in WA (Zone 11) during 2006, mint was irrigated with endothall-treated water using overhead sprinklers (Table B.1.1). The irrigation water was treated with endothall (2.0 lb ae/gal SC/L monoalkylamine salt) at a concentration of ~5 ppm, acid equivalent. The mint field was irrigated six times during vegetative development at RTIs of 7 days. A volume equivalent to ~1 acre inch of water (27,154 gal/A) was applied for each irrigation. Based on the concentration of the endothall and the amount of water applied, application rate for endothall was equivalent to 1.11 lb ae/A/application, for a total of 6.64 lb ae/A/season.

TABLE B.1.1. Study Use Pattern.							
Location (City, State; Year) Trial ID	End-Use Product	Application Information					
		Method; Timing	Concen. [1]	Volume (gal/A) [2]	Single Rate (lb ae/A) [3]	RTI [4] (days)	Total Rate (lb ae/A) [3]
Ephrata, WA 2006 WA$09	2.0 lb/gal SC	Six broadcast foliar application during vegetative development using overhead sprinklers.	4.97-5.00	26,715	1.11	7	6.64

[1] The concentrate of endothall (in acid equivalents) in the irrigation water. No adjuvants were included in the irrigation water.
[2] The target irrigation rate was 1 acre inch of water or 27,154 gal/A.
[3] The equivalent field use rates were calculated by the reviewer based on the concentration of the endothall (ae), the application volume and plot size.
[4] RTI = Retreatment Interval.

B.2. Sample Handling and Processing Procedures

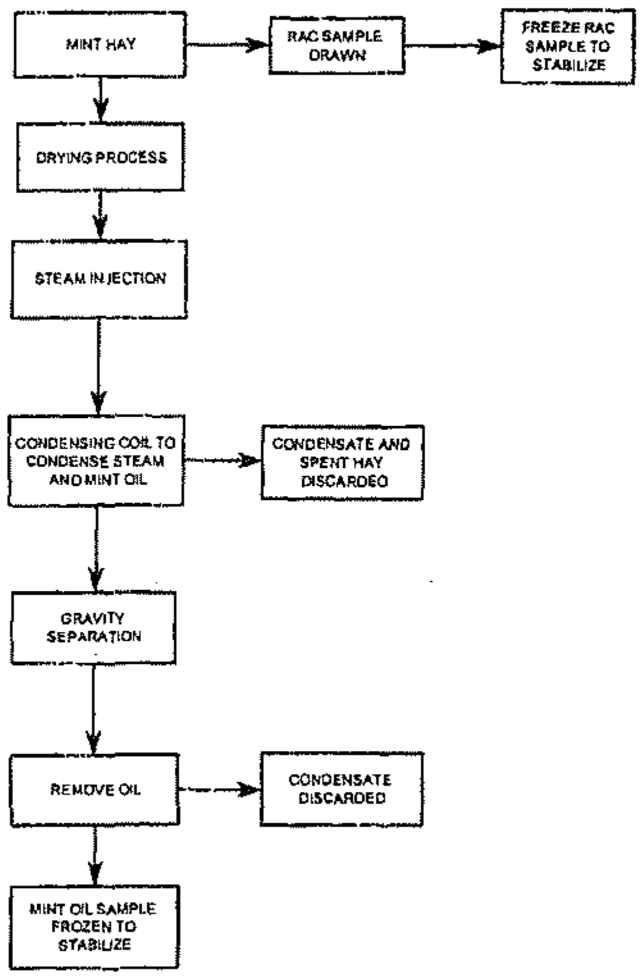
Single bulk control and treated samples of mint tops (≥134 lbs/sample) were harvested at 0 DAT, and were delivered fresh on the day after harvest by field personnel to the processing facility, Englar Food Laboratories, Inc. (Caldwell, ID). The samples were placed in cool storage 4 ± 3°C prior to processing, which was completed within 4 days of harvest.

The mint tops samples were processed according to simulated commercial procedures into mint oil (Figure B.1). The mint was placed in a modified steam retort and steam was injected through the bed for 1-2 hours. The condensate was collected and a layer of mint oil formed on the top of the condensate. The mint oil was condensed and separated from the water. Samples were placed in frozen storage -17°C immediately after processing. Samples were shipped frozen approximately 1 month after the completion of processing to the analytical laboratory, United Phosphorous, Inc., (King of Prussia, PA) via ACDS freezer truck. At the analytical laboratory, the samples were stored frozen (≤-18°C) prior to analysis.

FIGURE B.1. Processing Flowchart for Mint.

MINT PROCESSING

PILOT PLANT LABORATORY PROCESS



UNIVERSITY OF IDAHO FOOD TECHNOLOGY CENTER. 1908 E CHICAGO ST., CALDWELL ID 83605 208-455-9650
MINT PROCESSING FLOW CHART
THIS FLOW CHART IS THE PROPERTY OF ENGLAR FOOD LABORATORIES, INC. AND SHALL NOT BE DUPLICATED IN WHOLE OR IN PART OR USED FOR ANY PURPOSE OTHER THAN THAT PROVIDED, WITHOUT THE WRITTEN CONSENT OF EFL.

B.3. Analytical Methodology

Residues of the free acid of endothall in/on mint tops and oil were determined using a LC/MS/MS method (Method No. KP-242R1) entitled "Analytical Method for Determination of Endothall in Crops", issued 5/4/2007.

For this method, residues in/on mint tops were extracted twice by homogenization with water followed by centrifugation and filtering. The oil samples are mixed with water and then partitioned 3x with hexane, discarding the hexane phases. Residue in the resulting water fractions from both matrices were then derivatized with HFTH in 50% H_3PO_4 at 100-120°C for 90 minutes. After cooling, the derivatized residues were partitioned into MTBE, evaporated to dryness, and reconstituted in hexane:MTBE (1:1 v:v). Residues were then cleaned using an amine SPE cartridge eluted with methanol:MTBE (1:4). Residues were analyzed by LC/MS/MS using external standards. The m/z 397→166 ion transition was used for quantifying residues, and residues are expressed in acid equivalents. The validated LOQ for endothall is 0.05 ppm in mint tops and oil, and the estimated LOD is 0.0001 ppm.

For method validation, control samples of mint tops and oil were fortified with endothall at 0.05-5.0 ppm. For concurrent recoveries, control sample were fortified with endothall at 0.05-4.0 ppm for mint tops and at 0.05 and 1.0 ppm for mint oil.

C. RESULTS AND DISCUSSION

The LC/MS/MS method used for determining residues of endothall in/on mint tops and oil was adequately validated prior to and in conjunction with the analysis of field trial samples. Method validation recoveries averaged 78% with a standard deviation of 8% for mint tops and 74% with a standard deviation of 3% for mint oil (Table C.1). Concurrent recoveries averaged 79% with a standard deviation of 6% for mint tops and 83% (n=2) for mint oil. Apparent residues of endothall were <LOQ in/on control samples. Adequate sample calculations and example chromatograms were provided and the fortification levels used for method recoveries were similar in magnitude to the measured residue levels.

Samples of mint tops and oil were stored frozen at ≤-17°C for up to 336 days prior to analysis, and mint oil samples were stored up to 241 days (Table C.2). Adequate storage stability data are available indicating that endothall is stable under frozen storage conditions for up to 469 days in lettuce and for up to 306 days in soybean oil (47520719.der, under review). These stability data will support the storage durations and conditions for the mint processing study.

Following six overhead sprinkler applications of endothall (monoalkylamine salt) to mint at rates totaling 6.64 lb ae/A, residues in mint tops (RAC) were 3.96 ppm (Table C.3). Residues in oil were ND (<0.0001 ppm), resulting a processing factor of <0.001x.

TABLE C.1. Summary of Method Validation and Concurrent Recoveries of Endothall from Mint.

Matrix	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean ± Std. Dev. (%)
Method Validation				
Tops	0.05	3	74, 72, 71	72 ± 2
	0.5	3	72, 72, 74	73 ± 2
	5.0	3	85, 90, 90	88 ± 3
	Total	**9**	**71-90**	**78 ± 8**
Mint oil	0.05	3	70, 70, 72	71 ± 1
	0.5	3	76, 74, 74	75 ± 1
	5.0	3	80, 78, 75	78 ± 3
	Total	**9**	**70-80**	**74 ± 3**
Concurrent Recoveries				
Tops	0.05	2	85, 78	82
	2.0	1	72	72
	4.0	1	82	82
	Total	**4**	**72-85**	**79 ± 6**
Mint Oil	0.05	1	78	83
	1.0	1	87	

1 Standard deviations are calculated for data sets having ≥3 values.

TABLE C.2. Summary of Storage Conditions.

Matrix	Storage Temperature (°C)	Actual Storage Duration (days)[1]	Interval of Demonstrated Storage Stability (days)[2]
Tops	≤-17	22-336	467
Oil		241	306

1 Interval from harvest to extraction for analysis. Samples were extracted up to 4 days prior to analysis.
2 Endothall is stable under frozen storage conditions for up to 469 days in lettuce and 306 days in soybean oil (47520719.der under review).

TABLE C.3. Residue Data from Mint Processing Study with Endothall.

RAC	Processed Commodity	Total Rate[1]		PHI (days)	Residues (ppm)[2]	Processing Factor
		ppm	lb ae/A			
Mint	Tops (RAC)	5.0	6.64	0	3.96	--
	Oil				ND	<0.001x

1 The rate is expressed both in terms of the concentration in the irrigation water (ppm) and the total amount (lb ae/A) applied.
2 Expressed in acid equivalents. The LOQ is 0.05 ppm and the estimated LOD is 0.0001 ppm.
ND = not detected.

D. CONCLUSION

The mint processing study is adequate. Endothall residues are reduced in mint oil (<0.001x).

E. REFERENCES

None

F. DOCUMENT TRACKING

RDI: David Soderberg (5 June 2009); William Donovan (5 June 2009).
Petition Number: 8E7419
DP#: 356315
PC Code: 038901 and 038905

Template Version June 2005

Primary Evaluator	David Soderberg, Chemist, RABV, HED	Date: 5 June 2009
Approved by	William Donovan, Senior Scientist, RABV, HED	Date: 5 June 2009

This DER was originally prepared under contract by Dynamac Corporation (1910 Sedwick Road, Building 100, Suite B, Durham, NC 27713; submitted 3/30/2009). The DER has been reviewed by the Health Effects Division (HED) and revised as needed for clarity, correctness and to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORT:

47520718. Arsenovic, M. (2008) Endothall (Hydrothol 191): Magnitude of the Residue on Rice: Lab Project Number: Z9761. Unpublished study prepared by Interregional Research Project No. 4. 323 pages.

EXECUTIVE SUMMARY:

Interregional Research Project No. 4 (IR-4) submitted field trial data reflecting the exposure of rice to endothall through the use of treated irrigation water. In four rice field trials conducted during 2007 in Zones 4, 6 and 10, a 2.0 lb ae/gal soluble concentrate (SC/L) formulation of endothall (monoalkylamine salt) was used to treat the irrigation water at a rate of 5 ppm ae. [In order to avoid the complications of different molecular weights for different salts, endothall concentrations are expressed as the free acid equivalents (ae).] The treated water was applied to the rice during grain development and maturation as six broadcast foliar applications using overhead sprinklers, at retreatment intervals (RTIs) of 6-8 days. A volume equivalent to ~1 acre inch of water (27,154 gal/A) was applied for each application. Based on the concentration of the endothall and the amount of water applied, the application rates for endothall were equivalent to 1.13 lb ae/A/application, for a total of 6.75-6.77 lb ae/A/season.

Single control and duplicate treated samples of rice grain and straw were harvested from each test on the day of the final application or one day later (0-1 DAT), and samples were stored at ≤-10°C for up to 99 days prior to analysis. Adequate storage stability data are available to support the duration and conditions of sample storage.

Residues of endothall (free acid) in/on rice grain and straw were determined using an adequate LC/MS/MS method (Method No. KP-242R1). For this method, residues were extracted with water and then derivatized with heptafluoro-*p*-tolylhydrazine (HFTH) in 50% H_3PO_4. The derivatized residues were cleaned up by partitioning into methyl t-butyl ether (MTBE) and elution through an amine solid phase extraction (SPE) cartridge. Residues were then analyzed by LC/MS/MS using external standards for quantitation. Residues are expressed in endothall acid equivalents. The validated limit of quantitation (LOQ) for endothall in/on rice grain and straw is 0.05 ppm.

Following six overhead sprinkler applications with irrigation water containing endothall at 5 ppm (6.75-6.77 lb ae/A/season), endothall residues were 0.69-1.22 ppm in/on four samples of rice grain and 0.94-2.61 ppm in/on four samples of rice straw harvested at 0-1 DAT. Average endothall residues were 1.01 ppm for grain and 1.90 ppm for straw, and the highest average field trial (HAFT) residues were 1.18 ppm for grain and 2.60 ppm for straw. No residue decline data was provided.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the rice field trial residue data are classified as scientifically acceptable. Although limited field trials were performed, these applications are expected to be conservative relative to actual inadvertent applications. The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document, DP# 356315.

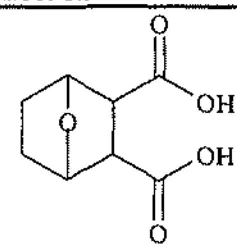
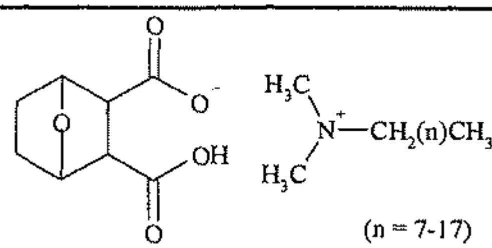
COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported which would have an adverse impact on the validity of the study.

A. BACKGROUND INFORMATION

Endothall [7-oxabicyclo[2,2,1] heptane-2,3-dicarboxylic acid] is a selective contact herbicide, defoliant, desiccant, and aquatic algaecide that belongs to the dicarboxylic acid chemical class. The free acid of endothall (PC Code 038901) and its dipotassium (PC Code 038904) and alkylamine (PC Code 038905) salts are registered primarily as aquatic herbicides for the control a variety of plants in water bodies. , including irrigation canals. They are also registered for desiccation/ defoliation of alfalfa/clover (grown for seed only), cotton, and potatoes prior to harvest, and for reduction of sucker branch growth in hops. Permanent tolerances are established for the combined residues of endothall and its monomethyl ester at 0.1 ppm in/on cotton seeds, fish, dried hops and potatoes, and at 0.05 ppm in/on rice grain and straw [40 CFR §180.293(a)(1)].

In conjunction with a petition for tolerances on a wide variety of irrigated crops (PP# 8E7419), IR-4 has submitted field trial data reflecting irrigation of rice with endothall-treated water. The chemical structure and nomenclature of endothall and its monoalkylamine salt are listed in Table A.1. The physicochemical properties of technical grade endothall and its monoalkylamine salt are listed in Table A.2.

Table A.1. Nomenclature of Endothall and its Monoalkylamine Salt.	
Chemical Structure	
Common name	Endothall
Molecular Formula	$C_8H_{10}O_5$
Molecular Weight	186.16
IUPAC name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid
CAS name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid
CAS #	145-73-3
PC Code	038901
Current Food/Feed Site Registration	Cotton, hops, potato, alfalfa grown for seed
Chemical Structure	
Common name	Endothall, mono-N,N-dimethylalkyl amine salt
Molecular Formula	Not available
Molecular Weight	Average: 422
IUPAC name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid, compound with N,N-dimethylcocoamine
CAS name	Not available
CAS #	66330-88-9
PC Code	038905
Current Food/Feed Site Registration	Cotton, hops, potato, alfalfa grown for seed, aquatic uses

23128

Table A.2. Physicochemical Properties of Endothall and Its Monoalkylamine Salt.		
Parameter	Value	Reference
Endothall (acid)		
Melting point	108-110℃	D187593, D187590, and D187588, 5/5/93, K. Dockter
pH	2.7 at 25℃ (1% solution)	D187593, D187590, and D187588, 5/5/93, K. Dockter
Density, bulk density, or specific gravity	0.481 g/cm^3 (bulk) at 25℃	D187593, D187590, and D187588, 5/5/93, K. Dockter
Water solubility at 25℃	109.8 g/L 13.1 g/100 mL in water, pH 5 12.7 g/100 mL in water, pH 7 12.5 g/100 mL in water, pH 9	D166798, 7/2/92, K. Dockter D207011, 9/30/94, F. Toghrol
Solvent solubility at 25℃	3.4 g/100 mL in acetonitrile 2.4 g/100 mL in n-octanol 16.0 g/100 mL in tetrahydrofuran	D207011, 9/30/94, F. Toghrol
Vapor pressure	3.92 x 10^{-5} mm Hg at 24.3℃	D166798, 7/2/92, K. Dockter
Dissociation constant, pK$_a$	4.32 for Step 1 and 6.22 for Step 2 at 20℃ (0.2% solution in 20% basic ethanol); dissociation rate 1.8-2.3 x 10^3 μmho within 3-5 minutes at □25℃, by conductivity meter	D188708, 5/3/93, K. Dockter
Octanol/water partition coefficient	Not applicable to endothall acid	D166798, 7/2/92, K. Dockter
UV/visible absorption spectrum	Not available	
Endothall, mono-N,N-dimethylalkyl amine salt		
Boiling point	Not available	
pH	5.2 at 25℃ (1% solution)	D187593, D187590, and D187588, 5/5/93, K. Dockter
Density, bulk density, or specific gravity	1.028 g/mL at 25℃	D187593, D187590, and D187588, 5/5/93, K. Dockter
Water solubility at 25℃	≥49.2 g/100mL in water, pH 5 ≥51.6 g/100 mL in water, pH 7 ≥49.8 g/100 mL in water, pH 9	D210814, 8/9/95, S. Knizner
Solvent solubility at 25℃	≥102.5 g/100mL in acetonitrile ≥95.4 g/100 mL in n-octanol ≥104.3 g/100 mL in tetrahydrofuran	D210814, 8/9/95, S. Knizner
Vapor pressure	2.09 x 10^{-5} mm Hg at 25℃ (calculated; mixed mono- and dialkylamine (C8-C20))	D206344, 9/22/94, F. Toghrol
Dissociation constant, pK$_a$	4.24 for Step 1 and 6.07 for Step 2 at 20℃ for mixed mono- and dialkylamine (C8-C20) in acidified ethanol/water; dissociation complete □17 minutes (1.7 x 10^3 μmho) at 25℃	D198885, 4/7/94, F. Toghrol
Octanol/water partition coefficient	K_{OW} 2.097 at concentrations of 8.9 x 10^{-3} M and 8.9 x 10^{-4} M, at 25℃	D209995, 1/20/95, L. Edwards
UV/visible absorption spectrum	Not available	

B. EXPERIMENTAL DESIGN

B.1. Study Site Information

Four rice field trials were conducted in Zones 4, 6 and 10 during 2007 (Table B.1.1). The irrigation water used in each test was treated with endothall (2.0 lb ae/gal SC monoalkylamine salt) at a concentration of ~5 ppm, acid equivalent. The treated water was applied to the rice during grain development and maturation as six broadcast foliar applications using overhead sprinklers, at RTIs of 6-8 days. A volume equivalent to ~1 acre inch of water (~27,154 gal/A) was applied for each application. Based on the concentration of the endothall and the amount of water applied, application rates for endothall were equivalent to 1.13 lb ae/A/application, for a total of 6.75-6.77 lb ae/A/season (Table B.1.3). These applications are expected to be conservative relative to actual applications

TABLE B.1.1. Trial Site Conditions.

Trial Identification (City, State; Year)	Soil characteristics [1]			
	Type	%OM	pH	CEC (meq/100g)
East Bernard, TX 2007 TX$24	Sandy Clay Loam	0.3	6.1	6.4
Cheneyville, LA 2007 LA$25	Sandy Clay Loam	0.8	8.1	14.3
Newport, AR 2007 AR$26	Loam	1.3	6.5	5.9
Biggs, CA 2007 CA$27	Clay Loam	2.4	5.4	24.5

[1] These parameters are optional except in cases where their value affects the use pattern for the chemical.

TABLE B.1.2. Water Characterization.

Study site	Water characteristics				
	Type	Hardness/Salinity	pH	Turbidity	Dissolved OM
East Bernard, TX 2007 TX$24	Well	NR	NR	NR	NR
Cheneyville, LA 2007 LA$25	Well	NR	NR	NR	NR
Newport, AR 2007 AR$26	City water	NR	NR	NR	NR
Biggs, CA 2007 CA$27	Well	NR	NR	NR	NR

NR = not reported.

The actual temperature recordings and rainfall were typical for each site and no unusual weather conditions were reported. No additional irrigation was reported during the study period. The tests were conducted according to normal agricultural practices for the regions, and information was provided on maintenance pesticides and fertilizers used at each site. No information was provided on the characteristics of the water used for irrigation, other than the source (Table B.1.2).

TABLE B.1.3. Study Use Pattern.

Location (City, State; Year) Trial ID	End-Use Product	Application Information					
		Method; Timing	Concen. [1]	Volume (gal/A) [2]	Single Rate (lb ae/A) [3]	RTI [4] (days)	Total Rate (lb ae/A) [3]
East Bernard, TX 2007 TX$24	2.0 lb ae/gal SC/L	Six broadcast foliar application from heading through grain maturation using overhead sprinklers.	4.98-5.00	27,046-27,089	1.13	6-7	6.75
Cheneyville, LA 2007 LA$25	2.0 lb ae/gal SC/L	Six broadcast foliar application from heading through grain maturation using overhead sprinklers.	4.98-5.00	27,151	1.13	6-7	6.77
Newport, AR 2007 AR$26	2.0 lb ae/gal SC/L	Six broadcast foliar application from early flowering through grain maturation using overhead sprinklers.	5.0	27,135-27,163	1.13	7-8	6.76
Biggs, CA 2007 CA$27	2.0 lb ae/gal SC/L	Six broadcast foliar application from milk grain stage through grain maturation using overhead sprinklers.	5.0	27,149	1.13	6-8	6.76

[1] The concentration of endothall (in acid equivalents) in the irrigation water. No adjuvants were included in the irrigation water.
[2] The target irrigation rate was 1 acre inch of water or 27,154 gal/A.
[3] The equivalent field use rates were calculated by the reviewer based on the concentration of the endothall (ae), the application volume and plot size.
[4] RTI = Retreatment Interval.

TABLE B.1.4. Trial Numbers and Geographical Locations.

NAFTA Growing Zones [1]	Rice		
	Submitted	Requested	
		Canada	U.S.
1	--	--	--
2	--	--	--
3	--	--	--
4	2	--	7
5	--	--	1
6	1	--	2
7	--	--	--
8	--	--	--
9	--	--	--
10	1	--	2
11	--	--	--
12	--	--	--
13	--	--	--
Total	4	--	12

[1] Zones 1A, 5A and B, 7A and 14-20 were not included as the use is for U.S only.

B.2. Sample Handling and Preparation

Samples of rice grain and straw were harvested at 0 or 1 DAT. Duplicate control and treated samples (≥1.0 lbs/sample straw and ≥2.0 lb/sample grain) were collected from each test and placed in frozen storage at each test facility within 6.5 hours. Samples were stored frozen at the field sites for 3-22 days. Samples were then shipped by ACDS freezer truck to the analytical laboratory, ALS Laboratory Group (Edmonton, AB, Canada), and stored frozen (≤-10EC) prior to analysis.

B.3. Analytical Methodology

Residues of endothall (free acid) in/on rice grain and straw were determined using a LC/MS/MS method (Method No. KP-242R1) entitled "Analytical Method for Determination of Endothall in Crops", issued 5/4/2007.

For this method, residues were extracted three times by homogenization with water followed by centrifugation and filtering. Residues were then derivatized with HFTH in 50% H_3PO_4 at 100-120°C for 90 minutes. After cooling, the derivatized residues were partitioned into MTBE, evaporated to dryness, and reconstituted in hexane:MTBE (1:1 v:v). Residues were then cleaned using an amine SPE cartridge eluted with methanol. Residues were analyzed by LC/MS/MS using external standards. The m/z 397→166 ion transition was used for quantifying residues. Residues are expressed in endothall acid equivalents. The validated LOQ for endothall in/on grain and straw is 0.05 ppm. An LOD of 0.000025 ppm was reported; however, this value was the instrument LOD, rather than the LOD of residues in a control matrix.

The above method was validated prior to and in conjunction with the analysis of the field trial samples. Control samples of grain and straw were fortified with endothall at 0.05-5.0 ppm for both method validation and concurrent recoveries.

C. RESULTS AND DISCUSSION

The LC/MS/MS method used for determining residues of endothall in/on rice was adequately validated prior to and in conjunction with the analysis of field trial samples. The average method validation recoveries (±SD) were 80 ± 8% for rice grain and 95 ± 12% for rice straw (Table C.1). Average concurrent recoveries (±SD) were 81 ± 7% for grain and 77 ± 8% for straw. Apparent residues of endothall were <LOQ in/on control samples. Adequate sample calculations and example chromatograms were provided, and the fortification levels used for the method recoveries were similar in magnitude to the measured residue levels.

Samples of rice grain and straw were stored at <-10°C for up to 99 days prior to analysis (Table C.2). Adequate storage stability data are available indicating that endothall is stable under frozen storage conditions for up to 306-469 days in lettuce, tomatoes, sugar beet roots, corn grain, and soybean seed and oil. As these data indicate that endothall is stable on diverse plant matrices during frozen storage, these data will support the storage durations and conditions for the current rice field trials.

Following six overhead sprinkler applications with irrigation water containing endothall at 5 ppm (6.75-6.77 lb ae/A/season), endothall residues were 0.69-1.22 ppm in/on four samples of rice grain and 0.94-2.61 ppm in/on four samples of rice straw harvested at 0-1 DAT (Table C.3). Average endothall residues were 1.01 ppm for grain and 1.90 ppm for straw (Table C.4). The HAFT residues were 1.18 ppm for grain and 2.60 ppm for straw. No residue decline data was provided.

Common cultural practices were used to maintain plants, and the weather conditions and maintenance chemicals and fertilizer used in this study did not have a notable impact on the residue data. No phytotoxicity was noted at any of the test sites.

TABLE C.1. Summary of Method Validation and Concurrent Recoveries of Endothall from Rice.

Matrix	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean ± Std. Dev. (%)
Method Validation				
Grain	0.05	3	93, 88, 88	90 ± 3
	0.5	3	76, 77, 75	76 ± 1
	5.0	3	74, 75, 71	73 ± 2
	Total	9	71-93	**80 ± 8**
Straw	0.05	3	81, 74, 83	79 ± 5
	0.5	3	97, 103, 109	103 ± 6
	5.0	3	96, 102, 106	101 ± 5
	Total	9	**74-109**	**95 ± 12**
Concurrent Recoveries				
Grain	0.05	2	87, 85	86
	0.5	1	70	70
	5.0	1	80	80
	Total	4	70-87	**81 ± 7**
Straw	0.05	2	70, 70	70
	5.0	2	87, 80	83
	Total	4	70-87	77 ± 8

1 Standard deviations are calculated for data sets having ≥3 values.

TABLE C.2. Summary of Storage Conditions.

Matrix	Storage Temperature (°C)	Actual Storage Duration (days)[1]	Interval of Demonstrated Storage Stability (days)[2]
Grain	≤-10	64-90	306-469
Straw		73-99	

1 Interval from harvest to extraction for analysis. Extracts were stored 2-8 days prior to analysis.
2 Based on storage stability data from frozen tomatoes, lettuce, corn grain, sugar beet roots, and soybean seeds (47520719.der, under review).

TABLE C.3. Residue Data from Rice Field Trials with Endothall Monoalkylamine Salt (SC/L).

Trial ID (City, State; Year)	Zone	Crop; Variety	Matrix	Total Rate [1] ppm	Total Rate [1] lb ae/A	PHI (days)	Residues (ppm) [2,4]	
East Bernard, TX 2007 TX$24	6	Rice; Cocodrie	Grain	5.0	6.75	1	1.22	1.14
			Straw				1.99	2.24
Cheneyville, LA 2007 LA$25	4	Rice; Clearfield 161	Grain	5.0	6.77	0	1.16	1.19
			Straw				1.09	0.94
Newport, AR 2007 AR$26	4	Rice; Wells	Grain	5.0	6.76	0	0.818 [3]	0.694 [3]
			Straw				1.90	1.86
Biggs, CA 2007 CA$27	10	Rice; M-205	Grain	5.0	6.76	0	0.802 [3]	1.08
			Straw				2.59	2.61

[1] The rate is expressed both in terms of the concentration in the irrigation water (ppm) and the total amount (lb ae/A) applied.
[2] Expressed in acid equivalents. The LOQ is 0.05 ppm.
[3] Average of two injections.
[4] The two results for each field trial represent two samples taken from a single plot, not two plots.

TABLE C.4. Summary of Residue Data from Rice Field Trials with Endothall Monoamine Salt (SC/L)..

Commodity	Total Applic. Rate [1]	PHI (days)	Residue Levels (ppm) [2] n	Min.	Max.	HAFT [3]	Median (STMdR)	Mean (STMR)	Std. Dev.
Rice grain	5 ppm (6.75-6.77)	0-1	4	0.756	1.18	1.18	1.05	1.05	0.200
Rice Straw		0-1	4	1.02	2.6	2.6	1.90	1.90	0.66

[1] The value in parentheses is the total application rate in terms of lb ae/A.
[2] Residues are expressed in terms of the free acid. The LOQ is 0.05 ppm.
[3] HAFT = Highest Average Field Trial.

D. CONCLUSION

The available field trial data are adequate and support the use of endothall-treated water for irrigation of rice. The data support the use of endothall in irrigation water at a concentration of 5 ppm (ae), with no more that six applications per season and a minimum 7-day interval between applications to the water. Residues were determined on the rice at a 0-day PHI.

E. REFERENCES

None

F. DOCUMENT TRACKING

RDI: David Soderberg (5 June 2009); William Donovan (5 June 2009)
Petition Number: 8E7419
DP#: 356315
PC Codes: 038901 and 038905

Template Version June 2005

Primary Evaluator	David Soderberg, Chemist, RABV, HED	Date: 5 June 2009
Approved by	William Donovan, Senior Scientist, RABV, HED	Date: 5 June 2009

This DER was originally prepared under contract by Dynamac Corporation (1910 Sedwick Road, Building 100, Suite B, Durham, NC 27713; submitted 3/30/2009). The DER has been reviewed by the Health Effects Division (HED) and revised as needed for clarity, correctness and to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORT:

47520718. Arsenovic, M. (2008) Endothall (Hydrothol 191): Magnitude of the Residue on Rice: Lab Project Number: Z9761. Unpublished study prepared by Interregional Research Project No. 4. 323 pages.

EXECUTIVE SUMMARY:

Interregional Research Project No. 4 (IR-4) submitted a rice grain processing study reflecting the exposure of rice to endothall through the use of treated irrigation water. In a field trial conducted in TX (Zone 6) during 2007, a 2.0 lb ae/gal soluble concentrate (SC/L) formulation of endothall (monoalkylamine salt) was used to treat the irrigation water at a rate of 5 ppm ae. [In order to avoid the complications of different molecular weights for different salts, endothall concentrations are expressed as the free acid equivalents (ae).] The treated water was then applied using overhead sprinklers to rice as six broadcast foliar applications during grain development and maturation at retreatment intervals (RTIs) of 6-7 days. A volume equivalent to 1 acre inch of water (~27,154 gal/A) was applied for each application. Based on the concentration of the endothall in the irrigation water and the amount of water applied, the application rate for endothall was equivalent to 1.13 lb ae/A/application, for a total of 6.75 lb ae/A/season.

Single bulk control and treated samples of rice grain were harvested at normal crop maturity, one day after the last irrigation (1 day after treatment, DAT). The grain was processed into hulls, bran and polished rice using simulated commercial procedures. The grain and processed fraction samples were stored at ≤-10°C for up to 48 days prior to analysis. The sample storage intervals and conditions are supported by the available storage stability data.

Residues of endothall (free acid) in/on rice grain, bran and hulls were determined using an adequate LC/MS/MS method (Method No. KP-242R1). For this method, residues were extracted with water and then derivatized with heptafluoro-*p*-tolylhydrazine (HFTH) in 50% H_3PO_4. The derivatized residues were cleaned up by partitioning into methyl t-butyl ether (MTBE) and elution through an amine solid phase extraction (SPE) cartridge. Residues were then analyzed by LC/MS/MS using external standards for quantitation. Residues are expressed in endothall acid equivalents. The validated limit of quantitation (LOQ) for endothall in/on rice commodities is 0.05 ppm.

Following six sprinkler applications of endothall (monoalkylamine salt) to rice at rates totaling 6.75 lb ae/A, residues in whole grain (RAC) were 0.872 ppm at 1 DAT, and the residues in the processed fractions were 0.6 ppm for polished rice, 3.44 ppm for hulls and 2.03 ppm for bran. The resulting processing factors were 0.07x for polished rice, 3.9x for hulls and 2.3x for bran. The theoretical processing factors for rice are 5x for hulls and 7.7x for bran.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the rice processing study data are scientifically acceptable. The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document, DP# 356315.

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported which would have an adverse impact on the validity of the study.

A. BACKGROUND INFORMATION

Endothall [7-oxabicyclo[2,2,1] heptane-2,3-dicarboxylic acid] is a selective contact herbicide, defoliant, desiccant, and aquatic algaecide that belongs to the dicarboxylic acid chemical class. The free acid of endothall (PC Code 038901) and its dipotassium (PC Code 038904) and alkylamine (PC Code 038905) salts are registered primarily as aquatic herbicides for the control a variety of plants in water bodies. , including irrigation canals. They are also registered for desiccation/ defoliation of alfalfa/clover (grown for seed only), cotton, and potatoes prior to harvest, and for reduction of sucker branch growth in hops. Permanent tolerances are established for the combined residues of endothall and its monomethyl ester at 0.1 ppm in/on cotton seeds, fish, dried hops and potatoes, and at 0.05 ppm in/on rice grain and straw [40 CFR §180.293(a)(1)].

In conjunction with a petition for tolerances on a wide variety of irrigated crops (PP# 8E7419), IR-4 has submitted a processing study for rice reflecting irrigation of the rice crop with endothall-treated water. The chemical structure and nomenclature of endothall and its monoalkylamine salt are listed in Table A.1. The physicochemical properties of technical grade endothall and its monoalkylamine salt are listed in Table A.2.

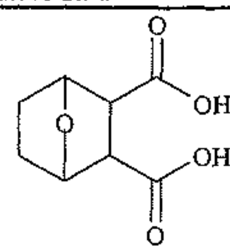
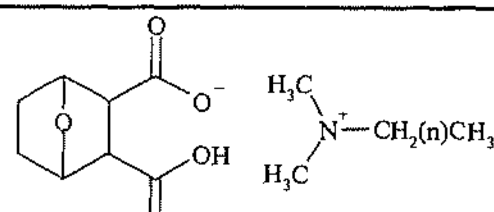
Table A.1. Nomenclature of Endothall and its Monoalkylamine Salt.	
Chemical Structure	
Common name	Endothall
Molecular Formula	$C_8H_{10}O_5$
Molecular Weight	186.16
IUPAC name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid
CAS name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid
CAS #	145-73-3
PC Code	038901
Current Food/Feed Site Registration	Cotton, hops, potato, alfalfa grown for seed
Chemical Structure	 (n = 7-17)
Common name	Endothall, mono-N,N-dimethylalkyl amine salt
Molecular Formula	Not available
Molecular Weight	Average: 422
IUPAC name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid, compound with N,N-dimethylcocoamine
CAS name	Not available
CAS #	66330-88-9
PC Code	038905
Current Food/Feed Site Registration	Cotton, hops, potato, alfalfa grown for seed, aquatic uses

Table A.2. Physicochemical Properties of Endothall and Its Monoalkylamine Salt.

Parameter	Value	Reference
Endothall (acid)		
Melting point	108-110°C	D187593, D187590, and D187588, 5/5/93, K. Dockter
pH	2.7 at 25°C (1% solution)	D187593, D187590, and D187588, 5/5/93, K. Dockter
Density, bulk density, or specific gravity	0.481 g/cm^3 (bulk) at 25°C	D187593, D187590, and D187588, 5/5/93, K. Dockter
Water solubility at 25°C	109.8 g/L 13.1 g/100 mL in water, pH 5 12.7 g/100 mL in water, pH 7 12.5 g/100 mL in water, pH 9	D166798, 7/2/92, K. Dockter D207011, 9/30/94, F. Toghrol
Solvent solubility at 25°C	3.4 g/100 mL in acetonitrile 2.4 g/100 mL in n-octanol 16.0 g/100 mL in tetrahydrofuran	D207011, 9/30/94, F. Toghrol
Vapor pressure	3.92 x 10^{-5} mm Hg at 24.3°C	D166798, 7/2/92, K. Dockter
Dissociation constant, pK$_a$	4.32 for Step 1 and 6.22 for Step 2 at 20°C (0.2% solution in 20% basic ethanol); dissociation rate 1.8-2.3 x 10^3 µmho within 3-5 minutes at □25°C, by conductivity meter	D188708, 5/3/93, K. Dockter
Octanol/water partition coefficient	Not applicable to endothall acid	D166798, 7/2/92, K. Dockter
UV/visible absorption spectrum	Not available	
Endothall, mono-N,N-dimethylalkyl amine salt		
Boiling point	Not available	
pH	5.2 at 25°C (1% solution)	D187593, D187590, and D187588, 5/5/93, K. Dockter
Density, bulk density, or specific gravity	1.028 g/mL at 25°C	D187593, D187590, and D187588, 5/5/93, K. Dockter
Water solubility at 25°C	≥49.2 g/100mL in water, pH 5 ≥51.6 g/100 mL in water, pH 7 ≥49.8 g/100 mL in water, pH 9	D210814, 8/9/95, S. Knizner
Solvent solubility at 25°C	≥102.5 g/100mL in acetonitrile ≥95.4 g/100 mL in n-octanol ≥104.3 g/100 mL in tetrahydrofuran	D210814, 8/9/95, S. Knizner
Vapor pressure	2.09 x 10^{-5} mm Hg at 25°C (calculated; mixed mono- and dialkylamine (C8-C20))	D206344, 9/22/94, F. Toghrol
Dissociation constant, pK$_a$	4.24 for Step 1 and 6.07 for Step 2 at 20°C for mixed mono- and dialkylamine (C8-C20) in acidified ethanol/water; dissociation complete □17 minutes (1.7 x 10^3 µmho) at 25°C	D198885, 4/7/94, F. Toghrol
Octanol/water partition coefficient	K_{OW} 2.097 at concentrations of 8.9 x 10^{-3} M and 8.9 x 10^{-4} M, at 25°C	D209995, 1/20/95, L. Edwards
UV/visible absorption spectrum	Not available	

B. EXPERIMENTAL DESIGN

B.1. Application and Crop Information

In a field trial conducted in TX (Zone 6) during 2007, rice was irrigated with endothall-treated water using overhead sprinklers (Table B.1.1). The irrigation water was treated with endothall (2.0 lb ae/gal SC/L monoalkylamine salt) at a concentration of ~5 ppm, acid equivalent. The rice field was irrigated six times during grain development and maturation at RTIs of 6-7 days. A volume equivalent to ~1 acre inch of water (27,154 gal/A) was applied for each irrigation. Based on the concentration of the endothall and the amount of water applied, application rate for endothall was equivalent to 1.13 lb ae/A/application, for a total of 6.75 lb ae/A/season.

TABLE B.1.1. Study Use Pattern.

Location (City, State; Year) Trial ID	End-Use Product	Application Information					
		Method; Timing	Concen. [1]	Volume (gal/A) [2]	Single Rate (lb ae/A) [3]	RTI [4] (days)	Total Rate (lb ae/A) [3]
East Bernard, TX 2007 TXS24	2.0 lb ae/gal SC/L	Six broadcast foliar application from heading through grain maturation using overhead sprinklers.	4.98-5.00	27,046-27,089	1.13	6-7	6.75

[1] The concentration of endothall (in acid equivalents) in the irrigation water. No adjuvants were included in the irrigation water.
[2] The target irrigation rate was 1 acre inch of water or 27,154 gal/A.
[3] The equivalent field use rates were calculated by the reviewer based on the concentration of the endothall (ae), the application volume and plot size.
[4] RTI = Retreatment Interval.

B.2. Sample Handling and Processing Procedures

Single control and treated bulk samples (≥147 lb/sample) of rice grain were harvested at 1 DAT, and were shipped by ACDS Freezer truck to the processing facility, GLP Technologies, Navasota, TX. Samples were placed in frozen storage ≤10°F prior to processing, which was completed within 21-25 days of harvest. Samples were processed using simulated commercial procedures into polished rice, hulls and bran (Figure B.1).

Rice grain samples were dried to a moisture content of 11-14%, and impurities were separated with a cleaner. The cleaned rice was hulled and debranned with a rice mill which removed the hull material and abraded away the bran to produce polished rice and bran. The bran was screened to remove hull material. Samples were transferred to frozen storage (≤-10°F) immediately after processing and were shipped frozen by overnight courier on dry ice 3 days after processing to ALS Laboratory Group (Edmonton, AB). At ALS, processed samples were stored frozen (≤-10EC) prior to analysis.

FIGURE B.1. Processing Flowchart for Rice Grain.

FORM H.210 Revision 00

RICE PROCESSING MATERIAL BALANCE

Sample # 2 (Treated, Trt. 02) Code # J

RICE 149.1 lbs.

Drying 129.8 lbs.

Screening 0.8 lbs. **LARGE SCREENINGS**
11.9 lbs. **SMALL SCREENINGS**

Aspiration 7.4 lbs. **LIGHT IMPURITIES**
109.5 lbs. **CLEANED RICE**

Dehulling 109.6 lbs. used

BROWN RICE 84.3 lbs. **HULL** 22.2 lbs

Debranning

BRAN 9.9 lbs **WHITE MILLED RICE** 64.1 lbs **UNHULLED SEED** 11.5 lbs

B.3. Analytical Methodology

Residues of endothall (free acid) in/on rice grain and straw were determined using a LC/MS/MS method (Method No. KP-242R1) entitled "Analytical Method for Determination of Endothall in Crops", issued 5/4/2007.

For this method, residues were extracted three times by homogenization with water followed by centrifugation and filtering. Residues were then derivatized with HFTH in 50% H_3PO_4 at 100-120°C for 90 minutes. After cooling, the derivatized residues were partitioned into MTBE, evaporated to dryness, and reconstituted in hexane:MTBE (1:1 v:v). Residues were then cleaned using an amine SPE cartridge eluted with methanol. Residues were analyzed by LC/MS/MS using external standards. The m/z 397→166 ion transition was used for quantifying residues.

Residues are expressed in endothall acid equivalents. The validated LOQ for endothall in/on grain and straw is 0.05 ppm. An LOD of 0.000025 ppm was reported; however, this value was the instrument LOD, rather than the LOD of residues in a control matrix.

The above method was validated prior to and in conjunction with the analysis of the field trial samples. Control samples of grain and straw were fortified with endothall at 0.05-5.0 ppm for both method validation and concurrent recoveries.

C. RESULTS AND DISCUSSION

The LC/MS/MS method used for determining residues of endothall in/on rice commodities was adequately validated prior to and in conjunction with the analysis of field trial samples. The average method validation recoveries (±SD) were 80 ± 8% for rice grain and 95 ± 12% for rice straw (Table C.1). Concurrent recoveries averaged 78% for grain and 75% for straw. Although no method recovery data were provided on polished rice, bran or hulls, the grain and straw recovery data are representative of hulls and bran. Apparent residues of endothall were <LOQ in/on control samples. Adequate sample calculations and example chromatograms were provided, and the fortification levels used for the method recoveries were similar in magnitude to the measured residue levels.

Samples of rice grain and grain processed fractions were stored at ≤-10°C for up to 48 days prior to analysis (Table C.2). Adequate storage stability data are available indicating that endothall is stable under frozen storage conditions for up to 306-469 days in lettuce, tomatoes, sugar beet roots, corn grain, and soybean seed and oil. As these data indicate that endothall is stable on diverse plant matrices during frozen storage, these data will support the storage durations and conditions for the current rice processing study.

Following six overhead sprinkler applications of endothall (monoalkylamine salt) to rice at rates totaling 6.75 lb ae/A, residues in whole grain (RAC) were 0.872 ppm at 1 DAT, and the residues in the resulting processed fractions were 0.6 ppm in polished rice, 3.44 ppm in hulls and 2.03 ppm in bran (Table C.3). The resulting processing factors were 0.07x for polished rice, 3.9x for hulls and 2.3x for bran. The theoretical processing factors for rice are 5x for hulls and 7.7x for bran.

TABLE C.1. Summary of Method Validation and Concurrent Recoveries of Endothall from Rice.

Matrix	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean ± Std. Dev. (%)
Method Validation				
Grain	0.05	3	93, 88, 88	90 ± 3
	0.5	3	76, 77, 75	76 ± 1
	5.0	3	74, 75, 71	73 ± 2
	Total	**9**	**71-93**	**80 ± 8**
Straw	0.05	3	81, 74, 83	79 ± 5
	0.5	3	97, 103, 109	103 ± 6
	5.0	3	96, 102, 106	101 ± 5
	Total	**9**	**74-109**	**95 ± 12**

TABLE C.1. Summary of Method Validation and Concurrent Recoveries of Endothall from Rice.				
Matrix	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean ± Std. Dev. (%)
Concurrent Recoveries				
Grain	0.05	1	85	78
	0.50	1	70	
Straw	0.05	1	70	75
	5.0	1	80	

[1] Standard deviations are calculated for data sets having ≥3 values.

TABLE C.2. Summary of Storage Conditions.			
Matrix	Storage Temperature (°C)	Actual Storage Duration (days)[1]	Interval of Demonstrated Storage Stability (days)[2]
Unprocessed rice	≤-10	43	466-469
Polished rice		39	
Hull		39	
Bran		48	

[1] Interval from harvest to extraction for analysis. Extracts were stored 2-11 days prior to analysis.

[2] Based on storage stability study with tomato, lettuce, corn grain, sugar beet roots, soybean oil and soybeans currently under review (MRID 47520719).

TABLE C.3. Residue Data from Rice Processing Study with Endothall Monoalkylamine Salt (SC/L).						
RAC	Processed Commodity	Total Rate [1]		PHI (days)	Residues (ppm) [2]	Processing Factor
		ppm	lb ae/A			
Rice	Whole grain (RAC)	5.0	6.75	t	0.872	--
	Polished rice				0.06	0.07x
	Hulls				3.44	3.9x
	Bran				2.03	2.3x

[1] The rate is expressed both in terms of the concentration in the irrigation water (ppm) and the total amount (lb ae/A) applied.

[2] Expressed in acid equivalents. The LOQ is 0.05 ppm.

D. CONCLUSION

The rice processing study is adequate. Endothall residues were reduced in polished grain (0.07x), but concentrated in hulls (3.9x) and bran (2.3x).

E. REFERENCES

None

F. DOCUMENT TRACKING

RDI: David Soderberg (5 June 2009); William Donovan (5 June 2009)
Petition Number: 8E7419
DP#: 356315
PC Codes: 038901 and 038905

Template Version June 2005

Primary Evaluator	David Soderberg, Chemist, RABV, HED	Date: 5 June 2009
Approved by	William H. Donovan William Donovan, Senior Scientist, RABV, HED	Date: 5 June 2009

This DER was originally prepared under contract by Dynamac Corporation (1910 Sedwick Road, Building 100, Suite B, Durham, NC 27713; submitted 3/30/2009). The DER has been reviewed by the Health Effects Division (HED) and revised as needed for clarity, correctness and to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORT:

47520705. Arsenovic, M. (2008) Endothall (Hydrothol 191): Magnitude of the Residue on Vegetable, Legume Group: Lab Project Number: Z9765. Z9765.07-ALS05 Unpublished study prepared by Interregional Research Project No. 4. 440 pages.

EXECUTIVE SUMMARY:

Interregional Research Project No. 4 (IR-4) submitted field trial data reflecting the exposure of representative legume vegetables to endothall through the use of treated irrigation water. A total of 10 tests were conducted in Zones 1, 4, 5, 10 and 12 during 2006-2007, including 2 tests on succulent podded beans, 2 tests on dry beans, 2 tests on succulent podded peas, and 4 tests on soybeans. In each test, a 2.0 lb ae/gal soluble concentrate (SC/L) formulation of endothall (monoalkylamine salt) was used to treat the irrigation water at a rate of 5 ppm ae. [In order to avoid the complications of different molecular weights for different salts, endothall concentrations are expressed as the free acid equivalents (ae).] The treated water was applied during flowering through pod and seed development as broadcast foliar applications using overhead sprinklers, at retreatment intervals (RTIs) of 6-9 days. A volume equivalent to ~1 acre inch of water (27,154 gal/A) was applied for each application. A total of six applications were made in each test, except in one of the succulent bean tests, which used eight applications. Based on the concentration of the endothall and the amount of water applied, the application rates for endothall were equivalent to 1.12-1.13 lb ae/A/application, for a total of 6.74-6.77 lb ae/A for the six applications or 9.02 lb ai/A for the eight applications.

Single control and duplicate treated samples of legume pods with seeds were harvested from the succulent bean and pea field trials and samples of dried seeds were harvested from the dry bean and soybean field trials. Samples were harvested on the day of the final application or one day later (0-1 DAT), and were stored at ≤-10°C for up to 431 days prior to analysis. Adequate storage stability data are available to support the duration and conditions of sample storage.

Residues of endothall (free acid) in/on legume vegetables were determined using an adequate LC/MS/MS method (Method No. KP-242R1). For this method, residues were extracted with water and then derivatized with heptafluoro-*p*-tolylhydrazine (HFTH) in 50% H_3PO_4. The derivatized residues were cleaned up by partitioning into methyl t-butyl ether (MTBE) and elution through an amine solid phase extraction (SPE) cartridge. Residues were then analyzed by LC/MS/MS using external standards for quantitation. Residues are expressed in endothall acid equivalents. The validated limit of quantitation (LOQ) for endothall in/on legume vegetables is 0.05 ppm, and the estimated limit of detection (LOD) was 0.0001 ppm.

Following repeated overhead sprinkler applications (6 or 8) with irrigation water containing endothall at 5 ppm ae (6.74-9.02 lb ae/A/season), endothall residues were 0.291-0.521 ppm ae in/on four samples of succulent podded beans, 0.522-1.00 ppm ae in/on four samples of succulent podded peas, 0.070-0.134 ppm ae in/on four samples of dried beans, and <0.05-0.072 ppm ae in/on 8 samples of soybeans harvested at 0-1 DAT. Average endothall residues were 0.388 ppm for succulent podded beans, 0.734 ppm for succulent podded peas, 0.109 ppm for dry beans, and 0.055 ppm for soybeans. The highest average field trial (HAFT) residues were 0.468 ppm for succulent podded beans, 0.939 ppm for succulent podded peas, 0.116 ppm for dry beans, and 0.070 ppm for soybeans. No residue decline data was provided.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the legume field trial residue data are scientifically acceptable. Although limited field trials were performed, these applications are expected to be conservative relative to actual inadvertent applications. The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document, DP# 356315.

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported which would have an adverse impact on the validity of the study.

A. BACKGROUND INFORMATION

Endothall [7-oxabicyclo[2,2,1] heptane-2,3-dicarboxylic acid] is a selective contact herbicide, defoliant, desiccant, and aquatic algaecide that belongs to the dicarboxylic acid chemical class. The free acid of endothall (PC Code 038901) and its dipotassium (PC Code 038904) and alkylamine (PC Code 038905) salts are registered primarily as aquatic herbicides for the control a variety of plants in water bodies. This includes irrigation canals, but only with a 7 day holding period. They are also registered for desiccation/ defoliation of alfalfa/clover (grown for seed only), cotton, and potatoes prior to harvest, and for reduction of sucker branch growth in hops. Permanent tolerances are established for the combined residues of endothall and its monomethyl ester at 0.1 ppm in/on cotton seeds, fish, dried hops and potatoes, and at 0.05 ppm in/on rice grain and straw [40 CFR §180.293(a)(1)].

In conjunction with a petition for tolerances on a wide variety of irrigated crops (PP# 8E7419), IR-4 has submitted field trial data reflecting irrigation of various legume vegetables with endothall-treated water. The chemical structure and nomenclature of endothall and its monoalkylamine salt are listed in Table A.1. The physicochemical properties of technical grade endothall and its monoalkylamine salt are listed in Table A.2.

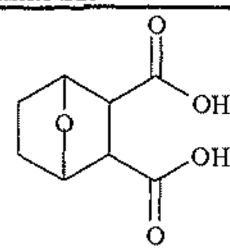
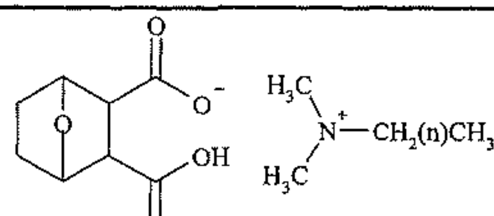
Table A.1. Nomenclature of Endothall and its Monoalkylamine Salt.	
Chemical Structure	
Common name	Endothall
Molecular Formula	$C_8H_{10}O_5$
Molecular Weight	186.16
IUPAC name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid
CAS name	7-oxabicyclo[2.2.1]hcptanc-2,3-dicarboxylic acid
CAS #	145-73-3
PC Code	038901
Current Food/Feed Site Registration	Cotton, hops, potato, alfalfa grown for seed
Chemical Structure	 (n = 7-17)
Common name	Endothall, mono-N,N-dimethylalkyl amine salt
Molecular Formula	Not available
Molecular Weight	Average: 422
IUPAC name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid, compound with N,N-dimethylcocoamine
CAS name	Not available
CAS #	66330-88-9
PC Code	038905
Current Food/Feed Site Registration	Cotton, hops, potato, alfalfa grown for seed, aquatic uses

Table A.2. Physicochemical Properties of Endothall and Its Monoalkylamine Salt.		
Parameter	Value	Reference
Endothall (acid)		
Melting point	108-110℃	D187593, D187590, and D187588, 5/5/93, K. Dockter
pH	2.7 at 25℃ (1% solution)	D187593, D187590, and D187588, 5/5/93, K. Dockter
Density, bulk density, or specific gravity	0.481 g/cm^3 (bulk) at 25℃	D187593, D187590, and D187588, 5/5/93, K. Dockter
Water solubility at 25℃	109.8 g/L 13.1 g/100 mL in water, pH 5 12.7 g/100 mL in water, pH 7 12.5 g/100 mL in water, pH 9	D166798, 7/2/92, K. Dockter D207011, 9/30/94, F. Toghrol
Solvent solubility at 25℃	3.4 g/100 mL in acetonitrile 2.4 g/100 mL in n-octanol 16.0 g/100 mL in tetrahydrofuran	D207011, 9/30/94, F. Toghrol
Vapor pressure	3.92 x 10^{-5} mm Hg at 24.3℃	D166798, 7/2/92, K. Dockter
Dissociation constant, pK$_a$	4.32 for Step 1 and 6.22 for Step 2 at 20℃ (0.2% solution in 20% basic ethanol); dissociation rate 1.8-2.3 x 10^3 μmho within 3-5 minutes at □25℃, by conductivity meter	D188708, 5/3/93, K. Dockter
Octanol/water partition coefficient	Not applicable to endothall acid	D166798, 7/2/92, K. Dockter
UV/visible absorption spectrum	Not available	
Endothall, mono-N,N-dimethylalkyl amine salt		
Boiling point	Not available	
pH	5.2 at 25℃ (1% solution)	D187593, D187590, and D187588, 5/5/93, K. Dockter
Density, bulk density, or specific gravity	1.028 g/mL at 25℃	D187593, D187590, and D187588, 5/5/93, K. Dockter
Water solubility at 25℃	≥49.2 g/100mL in water, pH 5 ≥51.6 g/100 mL in water, pH 7 ≥49.8 g/100 mL in water, pH 9	D210814, 8/9/95, S. Knizner
Solvent solubility at 25℃	≥102.5 g/100mL in acetonitrile ≥95.4 g/100 mL in n-octanol ≥104.3 g/100 mL in tetrahydrofuran	D210814, 8/9/95, S. Knizner
Vapor pressure	2.09 x 10^{-5} mm Hg at 25℃ (calculated; mixed mono- and dialkylamine (C8-C20))	D206344, 9/22/94, F. Toghrol
Dissociation constant, pK$_a$	4.24 for Step 1 and 6.07 for Step 2 at 20℃ for mixed mono- and dialkylamine (C8-C20) in acidified ethanol/water; dissociation complete □17 minutes (1.7 x 10^3 μmho) at 25℃	D198885, 4/7/94, F. Toghrol
Octanol/water partition coefficient	K_{OW} 2.097 at concentrations of 8.9 x 10^{-3} M and 8.9 x 10^{-4} M, at 25℃	D209995, 1/20/95, L. Edwards
UV/visible absorption spectrum	Not available	

B. EXPERIMENTAL DESIGN

B.1. Study Site Information

A total of 10 tests were conducted on representative legume vegetable crops in Zones 1, 4, 5, 10 and 12 during 2006-2007; including 2 tests on succulent podded beans, 2 tests on dry beans, 2 tests on succulent podded peas, and 4 tests on soybeans (Table B.1.1). The irrigation water used in each test was treated with endothall (2.0 lb ae/gal SC/L monoalkylamine salt) at a concentration of ~5 ppm, acid equivalent. The treated water was applied during flowering through pod and seed development as broadcast foliar applications using overhead sprinklers, at RTIs of 6-9 days. A volume equivalent to ~1 acre inch of water (~27,154 gal/A) was applied for each application. A total of six applications were made, except in one of the succulent bean tests (CA$26). Due to slow growth of the beans, a total of eight applications were made in the CA$26 test. Based on the concentration of the endothall and the amount of water applied, application rates for endothall were equivalent to 1.12-1.13 lb ae/A/application, for a total of 6.74-6.77 lb ae/A/season or 9.02 lb ae/A for the one site using having eight applications (Table B.1.3). These applications are expected to be conservative relative to actual applications.

TABLE B.1.1. Trial Site Conditions.

Trial Identification (City, State; Year)	Soil characteristics [1]			
	Type	%OM	pH	CEC (meq/100 g)
Succulent podded beans				
Arroyo Grande, CA 2007 CA$26	Sandy Loam	1.2	6.6	8.6
Baptistown, NJ 2006 NJ$24	Loam	2.3	6.7	9.1
Dried beans				
Delavan, WI 2007 WI$13	Silt Loam	2-4	5.6-7.8	6
Richland, IA 2007 IA$14	Silty Clay Loam	3.54	7.01	26.36
Succulent podded peas				
Ephrata, WA 2007 WA$17	Loamy Sand	0.8	7.7	11.7
Delavan, WI 2007 WI$12	Silt Loam	2-4	5.6-7.8	6
Soybeans				
Baptistown, NJ 2006 NJ$25	Loam	2.3	6.7	9.1
Newport, AR 2007 AR$16	Sandy Loam	1.1	6.3	5.6
Richland, IA 2007 IA$15	Silty Clay Loam	3.58	7.7	19.83
Sparta, IL 2007 IL$11	Silt Loam	2.7	7.5	12.5

[1] These parameters are optional except in cases where their value affects the use pattern for the chemical.

TABLE B.1.2. Water Characterization.

Study site	Water characteristics				
	Type	Hardness/Salinity	pH	Turbidity	Dissolved OM
Arroyo Grande, CA 2007 CA$26	Well	NR	NR	NR	NR
Baptistown, NJ 2006 NJ$24	Well	NR	NR	NR	NR
Delavan, WI 2007 WI$13	Rural water	NR	NR	NR	NR
Richland, IA 2007 IA$14	Well	NR	NR	NR	NR
Ephrata, WA 2007 WA$17	Well	NR	NR	NR	NR
Delavan, WI 2007 WI$12	Well	NR	NR	NR	NR
Baptistown, NJ 2006 NJ$25	Well	NR	NR	NR	NR
Newport, AR 2007 AR$16	City water	NR	NR	NR	NR
Richland, IA 2007 IA$15	Rural Water	NR	NR	NR	NR
Sparta, IL 2007 IL$11	City Water	NR	NR	NR	NR

NR = not reported.

The actual temperature recordings and rainfall were typical for each site and no unusual weather conditions were reported. No additional irrigation was reported during the study period. The tests were conducted according to normal agricultural practices for the regions, and information was provided on maintenance pesticides and fertilizers used at each site. No information was provided on the characteristics of the water used for irrigation, other than the source (Table B.1.2).

TABLE B.1.3. Study Use Pattern.							
Location (City, State; Year) Trial ID	End-Use Product	Application Information					
		Method; Timing	Concen. [1]	Volume (gal/A)	Single Rate (lb ae/A) [1]	RTI [4] (days)	Total Rate (lb ae/A) [3]
Succulent Beans w/ pods							
Arroyo Grande, CA 2007 CA$26	2.0 lb/gal SC	Eight broadcast foliar application from flowering through fruit maturation using overhead sprinklers.	5.00	27,149	1.13	7-9	9.02
Baptistown, NJ 2006 NJ$24	2.0 lb/gal SC	Six broadcast foliar application from flowering through fruit maturation using overhead sprinklers.	5.0	27,154	1.13	6-7	6.75
Dried Beans							
Delavan, WI 2007 WI$13	2.0 lb/gal SC	Six broadcast foliar application from flowering through fruit maturation using overhead sprinklers.	4.98	27,154	1.13	6-8	6.77
Richland, IA 2007 IA$14	2.0 lb/gal SC	Six broadcast foliar application from flowering through fruit maturation using overhead sprinklers.	5.00	27,154	1.13	6-8	6.77
Succulent Peas w/ pods							
Ephrata, WA 2007 WA$17	2.0 lb/gal SC	Six broadcast foliar application from flowering through fruit maturation using overhead sprinklers.	4.97	27,140	1.12	6-8	6.74
Delavan, WI 2007 WI$12	2.0 lb/gal SC	Six broadcast foliar application from flowering through fruit maturation using overhead sprinklers.	5.00	27,012-27,268	1.12-1.13	7	6.74
Dried Peas, Soybean							
Baptistown, NJ 2006 NJ$25	2.0 lb/gal SC	Six broadcast foliar application from flowering through fruit maturation using overhead sprinklers.	4.96-5.00	27,154	1.13	7	6.75
Newport, AR 2007 AR$16	2.0 lb/gal SC	Six broadcast foliar application from flowering through fruit maturation using overhead sprinklers.	5.00	27,142-27,159	1.13	6-8	6.76
Richland, IA 2007 IA$15	2.0 lb/gal SC	Six broadcast foliar application from flowering through fruit maturation using overhead sprinklers.	5.00	27,154	1.13	6-8	6.77
Sparta, IL 2007 IL$11	2.0 lb/gal SC	Six broadcast foliar application from flowering through fruit maturation using overhead sprinklers.	5.00	27,012	1.13	6-8	6.77

[1] The concentration of endothall (in acid equivalents) in the irrigation water. No adjuvants were included in the irrigation water.
[2] The target irrigation rate was 1 acre inch of water or 27,154 gal/A.
[3] The equivalent field use rates were calculated by the reviewer based on the concentration of the endothall (ae), the application volume and plot size.
[4] RTI = Retreatment Interval.

TABLE B.1.4. Trial Numbers and Geographical Locations.

NAFTA Growing Zones[4]	Succulent podded beans			Dried beans			Succulent podded Peas			Soybeans		
	Submitted	Requested[1]		Submitted	Requested[1]		Submitted	Requested[1]		Submitted	Requested[1]	
		Canada	U.S.		Canada	U.S.		Canada	U.S.		Canada	U.S.
1	1	--	--	--	--	--	--	--	1	1	--	--
2	--	--	3	--	--	--	--	--	--	--	--	2
3	--	--	--	--	--	--	--	--	1	--	--	--
4	--	--	--	--	--	--	--	--	--	1	--	2
5	--	--	1	2	--	4	1	--	3	2	--	11
6	--	--	--	--	--	--	--	--	--	--	--	--
7	--	--	--	--	--	1	--	--	--	--	--	--
8	--	--	--	--	--	1	--	--	--	--	--	--
9	--	--	--	--	--	1	--	--	--	--	--	--
10	1	--	1	--	--	1	--	--	--	--	--	--
11	--	--	1	--	--	1	--	--	1	--	--	--
12	--	--	--	--	--	--	1	--	1	--	--	--
13	--	--	--	--	--	--	--	--	--	--	--	--
Total	2	--	6[2]	2	--	9	2	--	6[1]	4	--	15

[1] Based on EPA OPPTS Guideline 860.1500.
[2] Twelve total field trials are required, six each for an edible podded bean and a succulent shelled bean
[2] Nine total field trials are required, three for an edible podded pea and six for a succulent shelled pea.
[4] Zones 1A, 5 A and B, 7A and 14-21 were not included as the proposed use is for the U.S. only.

B.2. Sample Handling and Preparation

Samples were harvested at 0 DAT (after the sixth or eighth application) except at one site (NJ$25) where harvest was delayed by one day (1 DAT) to allow the soybean plants to dry to facilitate threshing. Duplicate control and treated samples (≥2.0 lb/sample) were harvested from each site and placed in frozen storage at each test facility within 3 hours. Samples were stored frozen at the field sites for 6-46 days. Samples were then shipped by ACDS Freezer truck or overnight courier on dry ice to the analytical laboratory, ALS Laboratory Group (Edmonton, AB, Canada), and stored frozen (≤-10°C) prior to analysis.

B.3. Analytical Methodology

Residues of endothall (free acid) in/on succulent and dried legume vegetables were determined using a LC/MS/MS method (Method No. KP-242R1) entitled "Analytical Method for Determination of Endothall in Crops", issued 5/4/2007.

For this method, residues were extracted two times by homogenization with water followed by centrifugation and filtering. Residues were then derivatized with HFTH in 50% H_3PO_4 at 100-120°C for 90 minutes. After cooling, the derivatized residues were partitioned into MTBE, evaporated to dryness, and reconstituted in hexane:MTBE (1:1 v:v). Residues were then cleaned using an amine SPE cartridge eluted with methanol. Residues were analyzed by LC/MS/MS using external standards. The m/z 397→166 ion transition was used for quantifying residues.

Residues are expressed in endothall acid equivalents. The validated LOQ for endothall in/on legume vegetables is 0.05 ppm. The estimated LOD was 0.0001 ppm.

The above method was validated prior to and in conjunction with the analysis of the field trial samples. Control samples of soybeans (dried seed) and lima beans (succulent podded beans) were fortified with endothall at 0.05-5.0 ppm for method validation and at 0.05 and 0.5 ppm for concurrent recoveries.

C. RESULTS AND DISCUSSION

The LC/MS/MS method used for determining residues of endothall in/on legume vegetables was adequately validated prior to and in conjunction with the analysis of field trial samples. The average method validation recoveries (±SD) were 97 ± 16% for soybean seeds and 102 ± 18% for succulent podded lima beans (Table C.1). Average concurrent recoveries (±SD) were 86 ± 9% for soybeans and 96 ± 9% for succulent podded lima beans. Apparent residues of endothall were <LOQ in/on control samples. Adequate sample calculations and example chromatograms were provided and the fortification levels used for method recoveries were similar in magnitude to the measured residue levels.

Samples were stored frozen at ≤-10°C for 39-431 days prior to analysis (Table C.2). Adequate storage stability data are available indicating that endothall is stable under frozen storage conditions for up to 306-469 days in lettuce, tomatoes, sugar beet roots, corn grain, and soybean seeds and oil. These data will support the storage durations and conditions for the current legume field trials.

Following repeated overhead sprinkler applications (6 or 8) with irrigation water containing endothall at 5 ppm (6.75-9.02 lb ae/A/season), endothall residues were 0.291-0.521 ppm in/on four samples of succulent podded beans, 0.522-1.00 ppm in/on four samples of succulent podded peas, 0.070-0.134 ppm in/on four samples of dried beans, and <0.05-0.072 ppm in/on 8 samples of soybeans harvested at 0-1 DAT (Table C.3). Average endothall residues were 0.388 ppm for succulent podded beans, 0.734 ppm for succulent podded peas, 0.109 ppm for dry beans, and 0.055 ppm for soybeans (Table C.4). The HAFT residues were 0.468 ppm for succulent podded beans, 0.939 ppm for succulent podded peas, 0.116 ppm for dry beans, and 0.070 ppm for soybeans. No residue decline data was provided.

Common cultural practices were used to maintain plants, and the weather conditions and maintenance chemicals and fertilizer used in this study did not have a notable impact on the residue data. Chlorosis and necrosis of leaves from treated plants was reported in two field trials (IA and WA).

TABLE C.1. Summary of Method Validation and Concurrent Recoveries of Endothall from Legumes.

Matrix	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean ± Std. Dev. (%)
Method Validation				
Soybean seed (dried)	0.05	3	83, 76, 71	76 ± 6
	0.5	3	108, 101, 115	108 ±7
	5.0	3	104, 104, 113	107 ±5
	Total	9	**71-115**	**97 ± 16**
Lima Been (Succulent with pod)	0.05	3	81, 78, 79	79 ± 1
	0.5	3	111, 108, 120	113 ± 6
	5.0	3	118, 104, 119	114 ± 8
	Total	**9**	**78-120**	**102 ± 18**
Concurrent Recoveries				
Soybean seed (dried)	0.05	3	92, 99, 91	94 ± 4
	0.5	3	81, 75, 78	78 ± 3
	Total	**6**	**75-99**	**86 ± 9**
Lima Been (Succulent with pod)	0.05	2	98, 73	85
	0.5	2	84, 118	101
	Total	**4**	**73-118**	**93 ± 9**

1 Standard deviations were calculated only for datasets having ≥3 values.

TABLE C.2. Summary of Storage Conditions.

Matrix	Storage Temperature (°C)	Actual Storage Duration (days)[1]	Interval of Demonstrated Storage Stability (days)[2]
Lima beans	≤-10	93-431	315-469
Dried beans		63-76	
Garden peas		113-127	
Soybean seed		39-385	

1 Interval from harvest to extraction for analysis. Extracts were stored up to 15 days prior to analysis.
2 Based on storage stability data from frozen tomatoes, lettuce, corn grain, sugar beet roots, and soybean seeds (47520719.der, under review).

TABLE C.3. Residue Data from Crop Field Trials with Endothall Monoalkylamine Salt (SC/L).

Trial ID (City, State; Year)	Zone	Crop/Variety	Matrix	Total Rate[1] ppm	Total Rate[1] lb ae/A	PHI (days)	Residues (ppm)[2,3]	
Succulent Podded Beans								
Arroyo Grande, CA 2007 CA$26	10	Succulent Lima /speckled	Succulent seed w/pod	5.0	9.02	0	0.414	0.521
Baptistown, NJ 2006 NJ$24	1	Succulent Lima/ Burpee's Improved Bush	Succulent seed w/pod	5.0	6.75	0	0.291	0.324
Dried Beans								
Delavan, WI 2007 WI$13	5	Dry bean/ Pinto	Dried seed	5.0	6.77	0	0.134	0.070
Richland, IA 2007 IA$14	5	Dry bean/ Great Northern	Dried seed	5.0	6.77	0	0.109	0.123
Succulent Podded Peas								

TABLE C.3. Residue Data from Crop Field Trials with Endothall Monoalkylamine Salt (SC/L).								
Trial ID (City, State; Year)	Zone	Crop/Variety	Matrix	Total Rate [1]		PHI (days)	Residues (ppm) [2, 3]	
				ppm	lb ae/A			
Ephrata, WA 2007 WA$17	12	Succulent pea/ Tonic	Succulent seed w/pod	5.0	6.74	0	0.878	1.00
Delavan, WI 2007 WI$12	5	Succulent pea/ Wanto	Succulent seed w/pod	5.0	6.74	0	0.537	0.522
Soybean								
Baptistown, NJ 2006 NJ$25	1	Soybean/ 93244449	Dried seed	5.0	6.75	1	0.072	0.068
Newport, AR 2007 AR$16	4	Soybean/ BPR 5423 nRR	Dried seed	5.0	6.76	0	(0.017)	ND[4]
Richland, IA 2007 IA$15	5	Soybean/ 93M42	Dried seed	5.0	6.77	0	(0.020)	(0.017)
Sparta, IL 2007 IL$11	5	Soybean/ Asgrow AG 3905	Dried seed	5.0	6.77	0	(0.038)	(0.026)

[1] The rate is expressed both in terms of the concentration in the irrigation water (ppm) and the total amount (lb ae/A) applied.
[2] Expressed in endothall acid equivalents. The LOQ is 0.05 ppm and the estimated LOD is 0.0001 ppm. Values in parenthesis are <LOQ and ≥LOD.
[3] The two results for each field trial represent two samples taken from a single plot, not two plots.
[4] None Detected at the LOD

TABLE C.4. Summary of Residue Data from Legume Vegetable Field Trials with Endothall Monoamine Salt (SC/L).									
Commodity	Total Applic. Rate [1]	PHI (days)	Residue Levels (ppm) [2]						
			N	Min.	Max.	HAFT [3]	Median (STMdR)	Mean (STMR)	Std. Dev.
Succulent podded beans	5 ppm (6.75, 9.02) [4]	0	2	0.3075	0.4675	0.4675	0.3875	0.3875	0.113
Succulent podded peas	5 ppm (6.74)	0	2	0.5295	0.939	0.939	0.734	0.734	0.290
Dried Beans	5 ppm (6.77)	0	2	0.102	0.116	0.116	0.109	0.109	0.010
Soybean, dried seed	5 ppm (6.75-6.77)	0-1	4	<0.050	0.07	0.07	0.034	0.034	0.025

[1] The value in parentheses is the total application rate in terms of lb ae/A.
[2] Residues are expressed in terms of the free acid. The LOQ is 0.05 ppm. For values ≤LOQ, the LOQ was used for all calculations.
[3] HAFT = Highest Average Field Trial.
[4] One of the succulent podded bean field trials used 8 applications rather than 6 applications due to slow plant growth and maturation.

D. CONCLUSION

The available field trial data are adequate and support the use of endothall-treated water for irrigation of legume vegetables. The data support the use of endothall (monoalkylamine salt) in irrigation water at a concentration of 5 ppm (ae), with no more that six applications per season, and a minimum 7-day interval between applications to the water to vegetable crops. Crops were tested with a 0-day PHI.

E. REFERENCES

None

F. DOCUMENT TRACKING

RDI: David Soderberg (5 June 2009); William (5 June 2009
Petition Number: 8E7419
DP#: 356315
PC Code: 038901 and 038905

Template Version June 2005

Primary Evaluator	David Soderberg, Chemist, RABV, HED	Date: 5 June 2009
Approved by	William Donovan, Senior Scientist, RABV, HED	Date: 5 June 2009

This DER was originally prepared under contract by Dynamac Corporation (1910 Sedwick Road, Building 100, Suite B, Durham, NC 27713; submitted 3/27/2009). The DER has been reviewed by the Health Effects Division (HED) and revised as needed for clarity, correctness and to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORT:

47520706. Arsenovic, M. (2008) Endothall (Hydrothol 191): Magnitude of the Residue on Vegetable Fruiting Group: Lab Project Number: Z9766, Z9766.06-CA$28, Z9766.06-FL$27 Unpublished study prepared by Interregional Research Project No. 4. 180 pages.

EXECUTIVE SUMMARY:

Interregional Research Project No. 4 (IR-4) submitted field trial data reflecting the exposure of tomatoes to endothall through the use of treated irrigation water. In two tomato field trials conducted during 2006 in Zones 3 and 10, a 2.0 lb ae/gal soluble concentrate (SC/L) formulation of endothall (monoalkylamine salt) was used to treat the irrigation water at a rate of 5 ppm ae. [In order to avoid the complications of different molecular weights for different salts, endothall concentrations are expressed as the free acid equivalents (ae).] The treated water was applied to tomatoes during flowering and fruit development as six broadcast foliar applications using overhead sprinklers, at retreatment intervals (RTIs) of 6-8 days. A volume equivalent to ~1 acre inch of water (27,154 gal/A) was applied for each application. Based on the concentration of the endothall and the amount of water applied, the application rates for endothall were equivalent to 1.12-1.13 lb ae/A/application, for a total of 6.74-6.77 lb ae/A/season.

Single control and duplicate treated samples of tomatoes were harvested from each test on the day of the final application (0 days after treatment, DAT), and samples were stored at ≤-11°C for up to 106 days prior to analysis. Adequate storage stability data are available to support the duration and conditions of sample storage.

Residues of endothall (free acid) in/on tomatoes were determined using an adequate LC/MS/MS method (Method No. KP-242R1). For this method, residues were extracted with water and then derivatized with heptafluoro-*p*-tolylhydrazine (HFTH) in 50% H_3PO_4. The derivatized residues were cleaned up by partitioning into methyl t-butyl ether (MTBE) and elution through an amine solid phase extraction (SPE) cartridge. Residues were then analyzed by LC/MS/MS using external standards for quantitation. Residues are expressed in endothall acid equivalents. The validated limit of quantitation (LOQ) for endothall in/on tomatoes is 0.05 ppm.

Following six overhead sprinkler applications with irrigation water containing endothall at 5 ppm (6.74-6.77 lb ae/A/season), endothall residues at 0 DAT were <0.05 ppm in/on 4 samples of tomatoes.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the tomato field trial residue data are scientifically acceptable. Although only two field trials were performed, these applications are expected to be conservative relative to actual inadvertent applications. The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document, DP# 356315.

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported which would have an adverse impact on the validity of the study.

A. BACKGROUND INFORMATION

Endothall [7-oxabicyclo[2,2,1] heptane-2,3-dicarboxylic acid] is a selective contact herbicide, defoliant, desiccant, and aquatic algaecide that belongs to the dicarboxylic acid chemical class. The free acid of endothall (PC Code 038901) and its dipotassium (PC Code 038904) and alkylamine (PC Code 038905) salts are registered primarily as aquatic herbicides for the control a variety of plants in water bodies. . This includes irrigation canals, but only with a 7 day holding period. They are also registered for desiccation/ defoliation of alfalfa/clover (grown for seed only), cotton, and potatoes prior to harvest, and for reduction of sucker branch growth in hops. Permanent tolerances are established for the combined residues of endothall and its monomethyl ester at 0.1 ppm in/on cotton seeds, fish, dried hops and potatoes, and at 0.05 ppm in/on rice grain and straw [40 CFR §180.293(a)(1)].

In conjunction with a petition for tolerances on a wide variety of irrigated crops (PP# 8E7419), IR-4 has submitted field trial data reflecting irrigation of tomatoes with endothall-treated water. The chemical structure and nomenclature of endothall and its monoalkylamine salt are listed in Table A.1. The physicochemical properties of technical grade endothall and its monoalkylamine salt are listed in Table A.2.

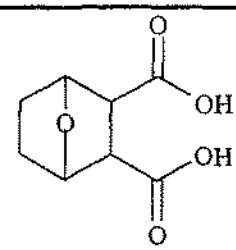
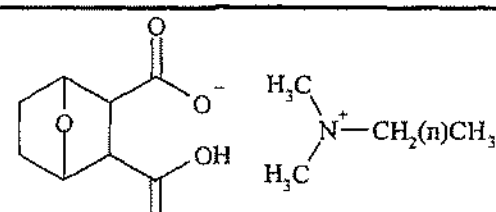
Table A.1. Endothall and Salts Nomenclature	
Chemical Structure	
Common name	Endothall
Molecular Formula	$C_8H_{10}O_5$
Molecular Weight	186.16
IUPAC name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid
CAS name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid
CAS #	145-73-3
PC Code	038901
Current Food/Feed Site Registration	Cotton, hops, potato, alfalfa grown for seed
Chemical Structure	 (n = 7-17)
Common name	Endothall, mono-N,N-dimethylalkyl amine salt
Molecular Formula	Not available
Molecular Weight	Average: 422
IUPAC name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid, compound with N,N-dimethylcocoamine
CAS name	Not available
CAS #	66330-88-9
PC Code	038905
Current Food/Feed Site Registration	Cotton, hops, potato, alfalfa grown for seed, aquatic uses

Table A.2. Physicochemical Properties of Endothall and Salts		
Parameter	Value	Reference
Endothall (acid)		
Melting point	108-110℃	D187593, D187590, and D187588, 5/5/93, K. Dockter
pH	2.7 at 25℃ (1% solution)	D187593, D187590, and D187588, 5/5/93, K. Dockter
Density, bulk density, or specific gravity	0.481 g/cm^3 (bulk) at 25℃	D187593, D187590, and D187588, 5/5/93, K. Dockter
Water solubility at 25℃	109.8 g/L 13.1 g/100 mL in water, pH 5 12.7 g/100 mL in water, pH 7 12.5 g/100 mL in water, pH 9	D166798, 7/2/92, K. Dockter D207011, 9/30/94, F. Toghrol
Solvent solubility at 25℃	3.4 g/100 mL in acetonitrile 2.4 g/100 mL in n-octanol 16.0 g/100 mL in tetrahydrofuran	D207011, 9/30/94, F. Toghrol
Vapor pressure	3.92 x 10^{-5} mm Hg at 24.3℃	D166798, 7/2/92, K. Dockter

Table A.2. Physicochemical Properties of Endothall and Salts		
Parameter	Value	Reference
Dissociation constant, pK_a	4.32 for Step 1 and 6.22 for Step 2 at 20℃ (0.2% solution in 20% basic ethanol); dissociation rate 1.8-2.3 x 10^3 μmho within 3-5 minutes at □25℃, by conductivity meter	D188708, 5/3/93, K. Dockter
Octanol/water partition coefficient	Not applicable to endothall acid	D166798, 7/2/92, K. Dockter
UV/visible absorption spectrum	Not available	
Endothall, mono-N,N-dimethylalkyl amine salt		
Boiling point	Not available	
pH	5.2 at 25℃ (1% solution)	D187593, D187590, and D187588, 5/5/93, K. Dockter
Density, bulk density, or specific gravity	1.028 g/mL at 25℃	D187593, D187590, and D187588, 5/5/93, K. Dockter
Water solubility at 25℃	≥49.2 g/100mL in water, pH 5 ≥51.6 g/100 mL in water, pH 7 ≥49.8 g/100 mL in water, pH 9	D210814, 8/9/95, S. Knizner
Solvent solubility at 25℃	≥102.5 g/100mL in acetonitrile ≥95.4 g/100 mL in n-octanol ≥104.3 g/100 mL in tetrahydrofuran	D210814, 8/9/95, S. Knizner
Vapor pressure	2.09 x 10^{-5} mm Hg at 25℃ (calculated; mixed mono- and dialkylamine (C8-C20))	D206344, 9/22/94, F. Toghrol
Dissociation constant, pK_a	4.24 for Step 1 and 6.07 for Step 2 at 20℃ for mixed mono- and dialkylamine (C8-C20) in acidified ethanol/water; dissociation complete □17 minutes (1.7 x 10^3 μmho) at 25℃	D198885, 4/7/94, F. Toghrol
Octanol/water partition coefficient	K_{OW} 2.097 at concentrations of 8.9 x 10^{-3} M and 8.9 x 10^{-4} M, at 25℃	D209995, 1/20/95, L. Edwards
UV/visible absorption spectrum	Not available	

B. EXPERIMENTAL DESIGN

B.1. Study Site Information

Two tomato field trials were conducted in Zones 3 and 10 during 2006 (Table B.1.1). The irrigation water used in each test was treated with endothall (2.0 lb ae/gal SC monoalkylamine salt) at a concentration of ~5 ppm, acid equivalent. The treated water was applied to the tomatoes during flowering and fruit development as six broadcast foliar applications using overhead sprinklers, RTIs of 6-8 days. A volume equivalent to ~1 acre inch of water (~27,000 gal/A) was applied for each application. Based on the concentration of the endothall and the amount of water applied, application rates for endothall were equivalent to 1.12-1.13 lb ae/A/application, for a total of 6.74-6.77 lb ae/A/season (Table B.1.3). These applications are expected to be conservative relative to actual applications.

TABLE B.1.1. Trial Site Conditions.				
Trial Identification (City, State; Year)	Soil characteristics[1]			
	Type	%OM	pH	CEC (meq/100g)
Grande Arroyo, CA 20006 CA$28	Sandy Loam	1.9	5.7	12.6
Oviedo, FL 2006 FL$27	Sand	0.7	6.3	3.1

[1]These parameters are optional except in cases where their value affects the use pattern for the chemical.

TABLE B.1.2. Water Characterization.					
Study site	Water characteristics				
	Type	Hardness/Salinity	pH	Turbidity	Dissolved OM
Grande Arroyo, CA 20006 CA$28	Well	NR	NR	NR	NR
Oviedo, FL 2006 FL$27	Artesian Well	NR	NR	NR	NR

NR = not reported.

The actual temperature recordings and rainfall were typical for each site and no unusual weather conditions were reported. Additional irrigation was supplied as needed using underground seep irrigation. The tests were conducted according to normal agricultural practices for the regions, and information was provided on maintenance pesticides and fertilizers used at each site. No information was provided on the characteristics of the water used for irrigation, other than the source (Table B.1.2).

TABLE B.1.3. Study Use Pattern.							
Location (City, State; Year) Trial ID	End-Use Product	Application Information					
		Method; Timing	Concen. [1]	Volume (gal/A) [2]	Single Rate (lb ae/A) [3]	RTI [4] (days)	Total Rate (lb ae/A) [3]
Grande Arroyo, CA 20006 CA$28	2.0 lb/gal SC	Six broadcast foliar application during flowering and fruit development using overhead sprinklers.	5.0	27,042	1.12	6-8	6.74
Oviedo, FL 2006 FL$27	2.0 lb/gal SC	Six broadcast foliar application during flowering and fruit development using overhead sprinklers.	5.0	27000	1.13	8	6.77

[1] The concentration of endothall (in acid equivalents) in the irrigation water. No adjuvants were included in the irrigation water.
[2] The target irrigation rate was 1 acre inch of water or 27,154 gal/A.
[3] The equivalent field use rates were calculated by the reviewer based on the concentration of the endothall (ae), the application volume and plot size.
[4] RTI = Retreatment Interval.

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TABLE B.1.4. Trial Numbers and Geographical Locations.

NAFTA Growing Zones	Tomatoes		
	Submitted	Requested[1]	
		Canada	U.S.
1	--	--	1
2	--	--	1
3	1	--	2
4	--	--	--
5	--	--	1
6	--	--	--
7	--	--	--
8	--	--	--
9	--	--	--
10	1	--	11 [7]
11	--	--	--
12	--	--	--
13	--	--	--
Total	2	--	16[12][2]

[1] Based on EPA OPPTS Guideline 860.1500.
[2] The number in brackets indicates a 25% reduction required to support a crop group tolerance.
[3] Zones 1A, 5 A and B, 7A and 14-21 were not included as the proposed use is for the U.S. only.

B.2. Sample Handling and Preparation

Duplicate control and treated samples (≥4 lb/sample, 12-24 fruits) of tomatoes were harvested at 0 DAT (after the sixth application) and placed in frozen storage at the test facility within 1 hour, 15 minutes. Samples were stored frozen at the field sites for 14 days prior to shipment by ACDS Freezer truck to the analytical laboratory (Cerexagri, Inc., King of Prussia, PA), and stored at ≤-11°C until analysis.

B.3. Analytical Methodology

Residues of endothall (free acid) in/on tomatoes were determined using a LC/MS/MS method (Method No. KP-242R1) entitled "Analytical Method for Determination of Endothall in Crops", issued 5/4/2007.

For this method, residues were extracted twice by homogenization with water followed by centrifugation and filtering. Residues were then derivatized with HFTH in 50% H_3PO_4 at 100-120°C for 90 minutes. After cooling, the derivatized residues were partitioned into MTBE, evaporated to dryness, and reconstituted in hexane:MTBE (1:1 v:v). Residues were then cleaned using an amine SPE cartridge eluted with methanol:MTBE (1:4). Residues were analyzed by LC/MS/MS using external standards. The m/z 397→166 ion transition was used for quantifying residues. Residues are expressed in endothall acid equivalents. The validated LOQ for endothall in/on tomatoes is 0.05 ppm, and the LOD was estimated to be 0.002 ppm.

The above method was validated prior to and in conjunction with the analysis of the field trial samples. Control samples of tomatoes were fortified with endothall at 0.05-5.0 ppm for method validation, and control samples were fortified with endothall at 0.05-1.0 ppm for concurrent recoveries.

C. RESULTS AND DISCUSSION

The LC/MS/MS method used for determining residues of endothall in/on tomatoes was adequately validated prior to and in conjunction with the analysis of field trial samples. Method validation recoveries averaged 89% with a standard deviation of 7%, and concurrent recoveries averaged 88% with a standard deviation of 15% (Table C.1). Apparent residues of endothall were <LOQ in/on control samples. Adequate sample calculations and example chromatograms were provided and the fortification levels used for method recoveries were similar in magnitude to the measured residue levels.

Tomato samples were stored frozen at ≤-11°C for up to 106 days prior to analysis (Table C.2). Adequate storage stability data are available indicating that endothall is stable in frozen tomatoes for up to 467 days (47520719.der, under review). These data will support the storage durations and conditions for the current field trials.

Following six overhead sprinkler applications with irrigation water containing endothall at 5 ppm (6.74-6.77 lb ae/A/season), endothall residues at 0 DAT were <0.05 ppm in/on 4 tomato samples (Table C.3). The average and HAFT residues were <0.05 ppm in/on tomatoes (Table C.4).

No phytotoxicity was noted on the treated tomato crops. Common cultural practices were used to maintain plants, and the weather conditions and maintenance chemicals and fertilizer used in this study did not have a notable impact on the residue data.

TABLE C.1. Summary of Method Validation and Concurrent Recoveries of Endothall from Tomato.

Matrix	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean ± Std. Dev. (%)
Method Validation				
Fruit	0.05	3	82, 79, 84	82 ± 3
	0.5	3	100, 92, 97	96 ± 4
	5.0	3	86, 93, 92	90 ± 4
	Total	**9**	79-100	89 ± 7
Concurrent Recoveries				
Fruit	0.05	2	104, 77	91
	0.5	1	98	98
	1.0	1	74	74
	Total	**4**	77-104	88 ± 15

[1] Standard deviations are calculated for data sets having ≥3 values.

TABLE C.2. Summary of Storage Conditions.			
Matrix	Storage Temperature (°C)	Actual Storage Duration (days)[1]	Interval of Demonstrated Storage Stability (days)[2]
Tomato RAC (fruit)	≤-11	77-106	467

[1] Interval from harvest to extraction for analysis. Extracts were stored up to 1 day prior to analysis.
[2] Endothall is stable in frozen tomatoes for up to 467 days (47520719.der under review).

TABLE C.3. Residue Data from Tomato Field Trials with Endothall Monoalkylamine Salt (SC/L).								
Trial ID (City, State; Year)	Zone	Crop/Variety	Matrix	Total Rate [1]		PHI (days)	Residues (ppm) [2, 3]	
				ppm	lb ae/A			
Grande Arroyo, CA 20006 CA$28	10	Tomato/ Organic Yaqui	Fruit	5.0	6.74	0	<0.05	<0.05
Oviedo, FL 2006 FL$27	3	Tomato/ Celebrity	Fruit	5.0	6.77	0	(0.027)[4]	(0.030)[4]

[1] The rate is expressed both in terms of the concentration in the irrigation water (ppm) and the total amount (lb ae/A) applied.
[2] Expressed in acid equivalents. The LOQ is 0.05 ppm and the LOD estimated to be 0.002 ppm.
[3] The two results for each field trial represent two samples taken from a single plot, not two plots.
[4] Results in parentheses are below the LLMV, but above the LOD.

TABLE C.4. Summary of Residue Data from Tomato Field Trials with Endothall Monoamine Salt (SC/L).									
Commodity	Total Applic. Rate [1]	PHI (days)	Residue Levels (ppm) [2]						
			N	Min.	Max.	HAFT [3]	Median (STMdR)	Mean (STMR)	Std. Dev.
Tomato	5 ppm (6.74-6.77)	0	2	<0.05	<0.05	<0.05	0.05	0.05	N/A

[1] The value in parentheses is the total application rate in terms of lb ae/A.
[2] Residues are expressed in terms of the free acid. The LOQ is 0.05 ppm. For all values reported ≤LOQ, the LOQ was used for all calculations.
[3] HAFT = Highest Average Field Trial.

D. CONCLUSION

The available field trial data are adequate and support the use of endothall-treated water for irrigation of tomatoes. The data support the use of endothall in irrigation water at a concentration of 5 ppm ae, with no more that six applications per season, and a minimum 7-day interval between applications to the water. Residues are determined at a 0-day PHI.

E. REFERENCES

None

F. DOCUMENT TRACKING

RDI: David Soderberg (5 June 2009); William Donovan (5 June 2009)
Petition Number: 8E7419
DP#: 356315
PC Code: 038901 and 038905

Template Version June 2005

Primary Evaluator	David Soderberg, Chemist, RABV, HED	Date: 5 June 2009
Approved by	William Donovan, Senior Scientist, RABV, HED	Date: 5 June 2009

This DER was originally prepared under contract by Dynamac Corporation (1910 Sedwick Road, Building 100 Suite B, Durham NC 27713; submitted 3/25/2009). The DER has been reviewed by the Health Effects Division (HED) and revised as needed for clarity, correctness and to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORT:

47520719. Fenn Li (2008) Stability of Endothall in Tomato, Lettuce, Sugar Beet Root and Corn grain, Soybean and Soybean Oil During Frozen Storage Pending Analysis: Lab Project Number: KP-2007-11. Unpublished study prepared by Interregional Research Project No. 4. 114 pages.

EXECUTIVE SUMMARY:

Frozen homogenized samples of tomato, lettuce, sugar beet root, corn grain, soybean seeds and oil were fortified with endothall (free acid) at 1.0 ppm and placed in storage at ≤-8°C. Four fortified replicates of each matrix were analyzed prior to storage on Day zero, and duplicate fortified samples of each matrix were reanalyzed after approximately 1, 10, and 15 months of frozen storage for tomato, lettuce, corn grain and sugar beet roots and after approximately 1, 5 and 10 months for soybean seeds and oil. At each sampling interval, control samples and two freshly fortified samples of each matrix were analyzed along with the stored samples.

Residues of endothall (free acid) in/on each plant commodity were determined using an adequate LC/MS/MS method (Method No. KP-242R1). For this method, residues were extracted with water and then derivatized with heptafluoro-*p*-tolylhydrazine (HFTH) in 50% H_3PO_4. The derivatized residues were cleaned up by partitioning into methyl t-butyl ether (MTBE) and elution through an amine solid phase extraction (SPE) cartridge. Residues were then analyzed by LC/MS/MS using external standards for quantitation. Residues are expressed in endothall acid equivalents. The reported limit of quantitation (LOQ) for endothall in/on plant commodities is 0.05 ppm, and the reported limit of detection (LOD) is 0.025 ppm.

The storage stability data indicate that endothall is stable at ≤-8°C for up to 465 days in tomatoes, lettuce, corn grain and sugar beet roots, and for up to 315 days in soybean seeds and oil. The corrected average recoveries from tomatoes, lettuce, corn grain and sugar beet roots were 99-112% at ~465 days and were 116-120% from soybean seeds and oil at ~315 days. The reported noted that the storage stability study on soybean seeds and oil is on-going.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the storage stability data are classified as scientifically acceptable. The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document, DP# 356315.

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported which would have an adverse impact on the validity of the study.

A. BACKGROUND INFORMATION

Endothall [7-oxabicyclo[2,2,1] heptane-2,3-dicarboxylic acid] is a selective contact herbicide, defoliant, desiccant, and aquatic algicide that belongs to the dicarboxylic acid chemical class. The free acid of endothall (PC Code 038901) and its dipotassium (PC Code 038904) and alkylamine (PC Code 038905) salts are registered primarily as aquatic herbicides for the control a variety of plants in water bodies. They are also registered for desiccation/defoliation of alfalfa/clover (grown for seed only), cotton, and potatoes prior to harvest, and for reduction of sucker branch growth in hops. Permanent tolerances are established for the combined residues of endothall and its monomethyl ester at 0. 1 ppm in/on cotton seeds, fish, dried hops and potatoes, and at 0.05 ppm in/on rice grain and straw [40 CFR §180.293(a)(1)].

In conjunction with a petition for tolerances on a wide variety of irrigated crops (PP# 8E7419), IR-4 has submitted storage stability data for a variety of plant matrices. The chemical structure and nomenclature of endothall are listed in Table A.1, and the physicochemical properties of technical grade endothall are listed in Table A.2.

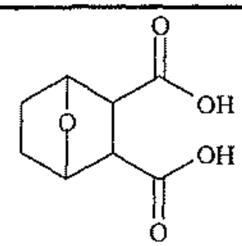
Table A.1. Endothall and Salts Nomenclature	
Chemical Structure	
Common name	Endothall
Molecular Formula	$C_8H_{10}O_5$
Molecular Weight	186.16
IUPAC name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid
CAS name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid
CAS #	145-73-3
PC Code	038901
Current Food/Feed Site Registration	Cotton, hops, potato, alfalfa grown for seed

Table A.2. Physicochemical Properties of Endothall.		
Parameter	Value	Reference
Melting point	108-110℃	D187593, D187590, and D187588, 5/5/93, K. Dockter
pH	2.7 at 25℃ (1% solution)	D187593, D187590, and D187588, 5/5/93, K. Dockter
Density, bulk density, or specific gravity	0.481 g/cm^3 (bulk) at 25℃	D187593, D187590, and D187588, 5/5/93, K. Dockter
Water solubility at 25℃	109.8 g/L 13.1 g/100 mL in water, pH 5 12.7 g/100 mL in water, pH 7 12.5 g/100 mL in water, pH 9	D166798, 7/2/92, K. Dockter D207011, 9/30/94, F. Toghrol
Solvent solubility at 25℃	3.4 g/100 mL in acetonitrile 2.4 g/100 mL in n-octanol 16.0 g/100 mL in tetrahydrofuran	D207011, 9/30/94, F. Toghrol
Vapor pressure	3.92 x 10^{-5} mm Hg at 24.3℃	D166798, 7/2/92, K. Dockter
Dissociation constant, pK$_a$	4.32 for Step 1 and 6.22 for Step 2 at 20℃ (0.2% solution in 20% basic ethanol); dissociation rate 1.8-2.3 x 10^3 μmho within 3-5 minutes at □25℃, by conductivity meter	D188708, 5/3/93, K. Dockter
Octanol/water partition coefficient	Not applicable to endothall acid	D166798, 7/2/92, K. Dockter
UV/visible absorption spectrum	Not available	

B. EXPERIMENTAL DESIGN

B.1. Sample Handling and Preparation

Frozen control samples of each matrix were obtained from other GLP studies, with the exception of soybean oil, which was purchased at a local store. The storage stability study was conducted at two different laboratories. Fortification and analysis of tomato, lettuce, sugar beet roots and corn grain was conducted by JFR America Laboratories (King of Prussia, PA), and the fortification and analysis of the soybean samples was conducted by ALS Laboratories (Edmonton, AB, Canada). All frozen control samples were homogenized prior to fortification, with the exception of soybean oil, for which homogenization was unnecessary.

For fortification, the endothall acid (monohydrate) was dissolved in either water (ALS lab) or acetone (JRF lab). Storage stability samples were prepared by fortifying a total of twenty-five 5g subsamples with endothall acid at 1.0 ppm.

B.2. Analytical Methodology

Residues of the free acid of endothall in/on each plant commodity were determined using a LC/MS/MS method (Method No. KP-242R1) entitled "Analytical Method for Determination of Endothall in Crops", issued 5/4/2007.

With the exception of soybean oil, residues were extracted twice by homogenization with water followed by centrifugation and filtering. For soybean oil, the sample was mixed with 5 mL of water and 3 mL of hexane and then centrifuged. Residues in the aqueous fraction were then derivatized with HFTH in 50% H_3PO_4 at 100-120°C for 90 minutes. After cooling, the derivatized residues were partitioned into MTBE, evaporated to dryness, and reconstituted in hexane:MTBE (1:1 v:v). Residues were then cleaned using an amine SPE cartridge eluted with methanol:MTBE (1:4). Residues were analyzed by LC/MS/MS using external standards. The m/z 397→166 ion transition was used for quantitation, and residues are expressed in acid equivalents. The reported LOQ and LOD for endothall in each commodity was 0.05 and 0.025 ppm, respectively.

This method was validated in conjunction with the analysis of the storage stability samples, using control samples of each commodity fortified with endothall at 1.0 ppm.

C. RESULTS AND DISCUSSION

Four fortified replicates of each matrix were analyzed prior to storage on Day 0, and duplicate fortified samples of each matrix were reanalyzed after approximately 1, 10, and 15 months of frozen storage for tomato, lettuce, corn grain and sugar beet roots and after approximately 1, 5 and 10 months for soybean seeds and oil. At each sampling interval, control samples and two freshly fortified samples of each matrix were analyzed along with the stored samples.

The LC/MS/MS method used for determining endothall residues was adequately validated in conjunction with the analysis of the storage stability samples. Average concurrent recoveries (±SD) were 83 ± 8% for tomatoes, 83 ± 11% for lettuce, 80 ± 9% for corn grain, 81 ± 11% for sugar beet roots, 88 ± 12% soybean seeds, and 94 ± 11% for soybean oil (Table C.1). Apparent residues of endothall were <LOQ in/on control samples. Adequate sample calculations and example chromatograms were provided.

The average corrected recoveries at all storage intervals were 93-104% for tomato, 100-118% for lettuce, 100-113% for corn grain, 99-108% for sugar beet roots, 99-116% for soybean seeds, and 93-120% for soybean oil (Table C.2)

TABLE C.1. Summary of Concurrent Recoveries of Endothall from Various Crops.

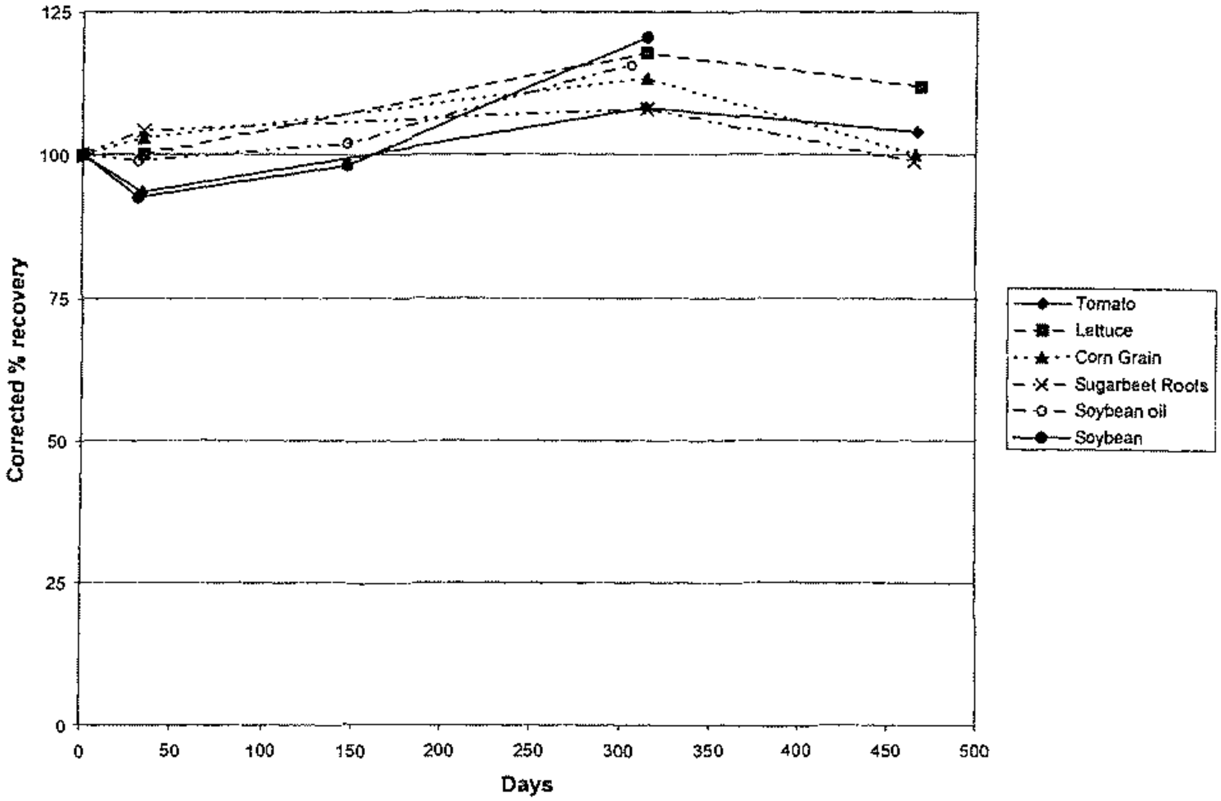
Matrix	Spike Level (ppm)	Storage Interval (days)	Sample Size (n)	Recoveries (%)	Mean ± Std. Dev. (%)
Tomato	1.0	0	4	91, 87, 91, 80	87
		33	2	88, 94	91
		314	2	73, 74	74
		467	2	79, 74	76
Lettuce	1.0	0	4	82, 82, 77, 81	80
		34	2	71, 76	74
		315	2	78, 80	79
		469	2	96, 108	102
Corn grain	1.0	0	4	93, 82, 90, 84	87
		34	2	70, 70	70
		315	2	75, 77	76
		466	2	88, 72	80
Sugar beet roots	1.0	0	4	73, 75, 104, 91	86
		34	2	70, 73	72
		315	2	76, 77	76

TABLE C.1.	**Summary of Concurrent Recoveries of Endothall from Various Crops.**				
Matrix	Spike Level (ppm)	Storage Interval (days)	Sample Size (n)	Recoveries (%)	Mean ± Std. Dev. (%)
		465	2	79, 90	84
Soybean oil	1.0	0	4	78, 80, 70, 80	77
		31	2	93, 88	90
		147	2	91, 114	102
		306	2	91, 90	90
Soybean seed	1.0	0	4	79, 104, 80, 98	90
		31	2	93, 94	94
		147	2	98, 116	107
		315	2	83, 92	88

TABLE C.2.	**Stability of Endothall Residues in Various Crops Following Storage at ≤-8°C.**					
Commodity	Spike Level (ppm)	Storage Interval (Days)	Recovered Residues (ppm)	Mean Recovered Residues (ppm)	Mean Recovery (%)	Corrected Recovery [1] (%)
Tomato	1.0	0	0.91, 0.87, 0.91, 0.80	0.87	87	N/A
		33	0.80, 0.90	0.85	85	93
		314	0.80, 0.80	0.80	80	108
		467	0.73, 0.85	0.79	79	104
Lettuce	1.0	0	0.82, 0.82, 0.77, 0.81	0.80	80	N/A
		34	0.71, 0.77	0.74	74	100
		315	0.93, 0.93	0.93	93	118
		469	1.14, 1.13	1.14	114	112
Corn grain	1.0	0	0.93, 0.82, 0.90, 0.84	0.87	87	N/A
		34	0.72, 0.72	0.72	72	103
		315	0.87, 0.86	0.86	86	113
		466	0.82, 0.77	0.80	80	100
Sugar beet roots	1.0	0	0.73, 0.75, 1.04, 0.91	0.86	86	N/A
		34	0.76, 0.74	0.75	75	104
		315	0.81, 0.82	0.82	82	108
		465	0.86, 0.80	0.83	83	99
Soybean oil	1.0	0	0.78, 0.80, 0.70, 0.80	0.77	77	N/A
		31	0.88, 0.90	0.89	89	99
		147	0.98, 109	1.04	104	102
		306	1.04, 1.04	1.04	104	116
Soybean seed	1.0	0	0.79, 1.04, 0.80, 0.98	0.90	90	N/A
		31	0.84, 0.90	0.87	87	93
		147	0.99, 1.11	1.05	105	98
		315	0.91, 1.20	1.06	106	120

[1] Corrected for mean concurrent recovery (see Table C.1.).

FIGURE C.1. Frozen Storage Stability of Endothall in Various Plant Matrices.



D. CONCLUSION

The storage stability data are adequate and indicate that endothall is stable at ≤-8°C for up to 465 days in tomatoes, lettuce, corn grain and sugar beet roots, and for up to 315 days in soybean seeds and oil. The storage stability study on soybean seeds and oil is on-going.

E. REFERENCES

None

F. DOCUMENT TRACKING

RDI: David Soderberg (5 June 2009); William Donovan (5 June 2009)
Petition Number: 8E7419
DP#:356315
PC Code: 038901

Template Version June 2005

Primary Evaluator	David Soderberg, Chemist, RABV, HED	Date: 5 June 2009
Approved by	William Donovan, Senior Scientist, RABV, HED	Date: 5 June 2009

This DER was originally prepared under contract by Dynamac Corporation (1910 Sedwick Road, Building 100, Suite B, Durham, NC 27713; submitted 3/27/2009). The DER has been reviewed by the Health Effects Division (HED) and revised as needed for clarity, correctness and to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORT:

47520709. Arsenovic, M. (2008) Endothall (Hydrothol 191): Magnitude of the Residue on Fruit, Pome Group: Lab Project Number: Z9767, Z9767.07-CER05 Unpublished study prepared by Interregional Research Project No. 4. 255 pages.

EXECUTIVE SUMMARY:

Interregional Research Project No. 4 (IR-4) submitted field trial data reflecting the exposure of apples to endothall through the use of treated irrigation water. In two apple field trials conducted during 2006 in Zones 1 and 11, a 2.0 lb ae/gal soluble concentrate (SC/L) formulation of endothall (monoalkylamine salt) was used to treat the irrigation water at a rate of 5 ppm ae. [In order to avoid the complications of different molecular weights for different salts, endothall concentrations are expressed as the free acid equivalents (ae).] The treated water was applied to the apple trees during fruit development as six broadcast foliar applications using overhead sprinklers, at retreatment intervals (RTIs) of 7 days. A volume equivalent to ~1 acre inch of water (27,154 gal/A) was applied for each application. Based on the concentration of the endothall and the amount of water applied, the application rates for endothall were equivalent to 1.11-1.13 lb ae/A/application, for a total of 6.64-6.79 lb ae/A/season.

Single control and duplicate treated samples of apples were harvested from each test on the day of the final application (0 days after treatment, DAT), and samples were stored at ≤-18°C for up to 203 days prior to analysis. Adequate storage stability data are available to support the duration and conditions of sample storage.

Residues of endothall (free acid) in/on apples were determined using an adequate LC/MS/MS method (Method No. KP-242R1). For this method, residues were extracted with water and then derivatized with heptafluoro-*p*-tolylhydrazine (HFTH) in 50% H_3PO_4. The derivatized residues were cleaned up by partitioning into methyl t-butyl ether (MTBE) and elution through an amine solid phase extraction (SPE) cartridge. Residues were then analyzed by LC/MS/MS using external standards for quantitation. Residues are expressed in endothall acid equivalents. The validated limit of quantitation (LOQ) for endothall in/on apples is 0.05 ppm.

Following six overhead sprinkler applications with irrigation water containing endothall at 5 ppm (6.64-6.79 lb ae/A/season), endothall residues at 0 DAT were <LOQ in/on 4 samples of apples, but were detectable at 0.031-0.047 ppm in 3 of the 4 samples. The average and highest average field trial (HAFT) residues were <0.05 ppm in/on apples.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the apple field trial residue data are scientifically acceptable. Although limited field trials were performed, these applications are expected to be conservative relative to actual inadvertent applications. The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document, DP# 356315.

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported which would have an adverse impact on the validity of the study.

A. BACKGROUND INFORMATION

Endothall [7-oxabicyclo[2,2,1] heptane-2,3-dicarboxylic acid] is a selective contact herbicide, defoliant, desiccant, and aquatic algaecide that belongs to the dicarboxylic acid chemical class. The free acid of endothall (PC Code 038901) and its dipotassium (PC Code 038904) and alkylamine (PC Code 038905) salts are registered primarily as aquatic herbicides for the control a variety of plants in water bodies. This includes irrigation canals, but only with a 7 day holding period. They are also registered for desiccation/ defoliation of alfalfa/clover (grown for seed only), cotton, and potatoes prior to harvest, and for reduction of sucker branch growth in hops. Permanent tolerances are established for the combined residues of endothall and its monomethyl ester at 0.1 ppm in/on cotton seeds, fish, dried hops and potatoes, and at 0.05 ppm in/on rice grain and straw [40 CFR §180.293(a)(1)].

In conjunction with a petition for tolerances on a wide variety of irrigated crops (PP# 8E7419), IR-4 has submitted field trial data reflecting irrigation of apples with endothall-treated water. The chemical structure and nomenclature of endothall and its monoalkylamine salt are listed in Table A.1. The physicochemical properties of technical grade endothall and its monoalkylamine salt are listed in Table A.2.

Table A.1. Nomenclature of Endothall and its Monoalkylamine Salt.

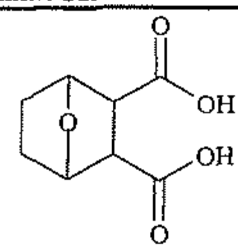
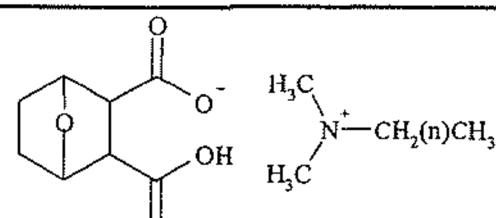
Chemical Structure	
Common name	Endothall
Molecular Formula	$C_8H_{10}O_5$
Molecular Weight	186.16
IUPAC name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid
CAS name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid
CAS #	145-73-3
PC Code	038901
Current Food/Feed Site Registration	Cotton, hops, potato, alfalfa grown for seed
Chemical Structure	 (n = 7-17)
Common name	Endothall, mono-N,N-dimethylalkyl amine salt
Molecular Formula	Not available
Molecular Weight	Average: 422
IUPAC name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid, compound with N,N-dimethylcocoamine
CAS name	Not available
CAS #	66330-88-9
PC Code	038905
Current Food/Feed Site Registration	Cotton, hops, potato, alfalfa grown for seed, aquatic uses

Table A.2. Physicochemical Properties of Endothall and Its Monoalkylamine Salt.

Parameter	Value	Reference
Endothall (acid)		
Melting point	108-110℃	D187593, D187590, and D187588, 5/5/93, K. Dockter
pH	2.7 at 25℃ (1% solution)	D187593, D187590, and D187588, 5/5/93, K. Dockter
Density, bulk density, or specific gravity	0.481 g/cm^3 (bulk) at 25℃	D187593, D187590, and D187588, 5/5/93, K. Dockter
Water solubility at 25℃	109.8 g/L 13.1 g/100 mL in water, pH 5 12.7 g/100 mL in water, pH 7 12.5 g/100 mL in water, pH 9	D166798, 7/2/92, K. Dockter D207011, 9/30/94, F. Toghrol
Solvent solubility at 25℃	3.4 g/100 mL in acetonitrile 2.4 g/100 mL in n-octanol 16.0 g/100 mL in tetrahydrofuran	D207011, 9/30/94, F. Toghrol
Vapor pressure	3.92×10^{-5} mm Hg at 24.3℃	D166798, 7/2/92, K. Dockter

Table A.2. Physicochemical Properties of Endothall and Its Monoalkylamine Salt.		
Parameter	Value	Reference
Dissociation constant, pK_a	4.32 for Step 1 and 6.22 for Step 2 at 20℃ (0.2% solution in 20% basic ethanol); dissociation rate 1.8-2.3 x 10^3 µmho within 3-5 minutes at □25℃, by conductivity meter	D188708, 5/3/93, K. Dockter
Octanol/water partition coefficient	Not applicable to endothall acid	D166798, 7/2/92, K. Dockter
UV/visible absorption spectrum	Not available	
Endothall, mono-N,N-dimethylalkyl amine salt		
Boiling point	Not available	
pH	5.2 at 25℃ (1% solution)	D187593, D187590, and D187588, 5/5/93, K. Dockter
Density, bulk density, or specific gravity	1.028 g/mL at 25℃	D187593, D187590, and D187588, 5/5/93, K. Dockter
Water solubility at 25℃	≥49.2 g/100mL in water, pH 5 ≥51.6 g/100 mL in water, pH 7 ≥49.8 g/100 mL in water, pH 9	D210814, 8/9/95, S. Knizner
Solvent solubility at 25℃	≥102.5 g/100mL in acetonitrile ≥95.4 g/100 mL in n-octanol ≥104.3 g/100 mL in tetrahydrofuran	D210814, 8/9/95, S. Knizner
Vapor pressure	2.09 x 10^{-5} mm Hg at 25℃ (calculated; mixed mono- and dialkylamine (C8-C20))	D206344, 9/22/94, F. Toghrol
Dissociation constant, pK_a	4.24 for Step 1 and 6.07 for Step 2 at 20℃ for mixed mono- and dialkylamine (C8-C20) in acidified ethanol/water; dissociation complete □17 minutes (1.7 x 10^3 µmho) at 25℃	D198885, 4/7/94, F. Toghrol
Octanol/water partition coefficient	K_{OW} 2.097 at concentrations of 8.9 x 10^{-3} M and 8.9 x 10^{-4} M, at 25℃	D209995, 1/20/95, L. Edwards
UV/visible absorption spectrum	Not available	

B. EXPERIMENTAL DESIGN

B.1. Study Site Information

Two apple field trials were conducted in Zones 1 and 11 during 2006 (Table B.1.1). The irrigation water used in each test was treated with endothall (2.0 lb ae/gal SC monoalkylamine salt) at a concentration of ~5 ppm, acid equivalent. The treated water was applied to the apple trees during fruit development as six broadcast foliar applications using overhead sprinklers, at RTIs of 7 days. A volume equivalent to ~1 acre inch of water (~27,154 gal/A) was applied for each application. Based on the concentration of the endothall and the amount of water applied, application rates for endothall were equivalent to 1.11-1.13 lb ae/A/application, for a total of 6.64-6.79 lb ae/A/season (Table B.1.3). These applications are expected to be conservative relative to actual applications.

TABLE B.1.1. Trial Site Conditions.				
Trial Identification (City, State; Year)	Soil characteristics[1]			
	Type	%OM	pH	CEC (meq/100g)
North Rose, NY 2006 NY$29	Sandy Loam	2.9	6.5	5.7
Ephrata, WA 2006 WA$16	Sandy Loam	0.9	7.9	13.6

[1]These parameters are optional except in cases where their value affects the use pattern for the chemical.

TABLE B.1.2. Water Characterization.					
Study site	Water characteristics				
	Type	Hardness/Salinity	pH	Turbidity	Dissolved OM
North Rose, NY 2006 NY$29	Well	NR	NR	NR	NR
Ephrata, WA 2006 WA$16	Well	NR	NR	NR	NR

NR= not reported.

The actual temperature recordings and rainfall were typical for each site. The petitioner noted that precipitation for the NY site was above normal during the growing period, but the moisture excess did not affect crop growth or have any negative impact on the trial. Additional irrigation was reported for the WA site, with under-tree micro-sprinklers. The tests were conducted according to normal agricultural practices for the regions, and information was provided on maintenance pesticides and fertilizers used at each site. No information was provided on the characteristics of the water used for irrigation, other than the source (Table B.1.2).

TABLE B.1.3. Study Use Pattern.							
Location (City, State; Year) Trial ID	End-Use Product	Application; no adjuvant used					
		Method; Timing	Concen. [1]	Volume (gal/A) [2]	Single Rate (lb ae/A) [3]	RTI [4] (days)	Total Rate (lb ae/A) [3]
North Rose, NY 2006 NY$29	2.0 lb/gal SC	Six broadcast foliar application during fruit development using overhead sprinklers.	5.01	27,089	1.13	7	6.79
Ephrata, WA 2006 WA$16	2.0 lb/gal SC	Six broadcast foliar application during fruit development using overhead sprinklers.	4.97-5.0	26,715	1.11	7	6.64

1 The concentration of endothall (in acid equivalents) in the irrigation water. No adjuvants were included in the irrigation water.
2 The target irrigation rate was 1 acre inch of water or 27,154 gal/A.
3 The equivalent field use rates were calculated by the reviewer based on the concentration of the endothall (ae), the application volume and plot size.
4 RTI = Retreatment Interval.

TABLE B.1.4. Trial Numbers and Geographical Locations.			
NAFTA Growing Zones[3]	Apple		
	Submitted	Requested[1]	
		Canada	U.S.
1	1	--	4
2	--	--	2
3	--	--	--
4	--	--	--
5	--	--	3
6	--	--	--
7	--	--	--
8	--	--	--
9	--	--	1
10	--	--	1
11	1	--	5
12	--	--	--
13	--	--	--
Total	2	--	16 [12][2]

[1] Based on EPA OPPTS Guideline 860.1500.
[2] The number in brackets indicates a 25% reduction required to support a crop group tolerance.
[3] Zones 1A, 5 A and B, 7A and 14-21 were not included as the proposed use is for the U.S. only.

B.2. Sample Handling and Preparation

Duplicate control and treated samples (≥8.25 lb/sample, 24 fruits) of apples were harvested at 0 DAT (after the sixth application) and placed in frozen storage at the test facility within 45 minutes. Samples were stored frozen at the field sites for 5-23 days prior to shipment by ACDS Freezer truck to the analytical laboratory (Cerexagri, Inc., King of Prussia, PA), and stored at ≤-18°C until analysis.

B.3. Analytical Methodology

Residues of endothall (free acid) in/on apples were determined using a LC/MS/MS method (Method No. KP-242R1) entitled "Analytical Method for Determination of Endothall in Crops", issued 5/4/2007.

For this method, residues were extracted twice by homogenization with water followed by centrifugation and filtering. Residues were then derivatized with HFTH in 50% H_3PO_4 at 100-120°C for 90 minutes. After cooling, the derivatized residues were partitioned into MTBE, evaporated to dryness, and reconstituted in hexane:MTBE (1:1 v:v). Residues were then cleaned using an amine SPE cartridge eluted with methanol:MTBE (1:4). Residues were analyzed by LC/MS/MS using external standards. The m/z 397→166 ion transition was used for quantifying residues. Residues are expressed in endothall acid equivalents. The validated LOQ for endothall in/on apples is 0.05 ppm, and the LOD was estimated to be 0.0025 ppm.

The above method was validated prior to and in conjunction with the analysis of the field trial samples. Control samples of apples were fortified with endothall at 0.05-5.0 ppm for method validation, and control samples were fortified with endothall at 0.05 ppm for concurrent recoveries.

C. RESULTS AND DISCUSSION

The LC/MS/MS method used for determining residues of endothall in/on apples was adequately validated prior to and in conjunction with the analysis of field trial samples. Method validation recovery averaged 88% with a standard deviation of 10%, and concurrent recoveries averaged 87% with a standard deviation of 13% (Table C.1). Apparent residues of endothall were non-detectable in/on control samples. Adequate sample calculations and example chromatograms were provided and the fortification levels used for method recoveries were similar in magnitude to the measured residue levels.

Apple samples were stored frozen at ≤-18°C for up to 230 days prior to analysis (Table C.2). Adequate storage stability data are available indicating that endothall is stable in frozen tomatoes for up to 467 days (47520719.der, under review). These data will support the storage durations and conditions for the current field trials.

Following six overhead sprinkler applications with irrigation water containing endothall at 5 ppm (6.74-6.77 lb ae/A/season), endothall residues at 0 DAT were <LOQ in/on 4 apple samples, but were detectable at 0.031-0.047 ppm in 3 of the 4 samples (Table C.3). The average and HAFT residues were <0.05 ppm in/on apples (Table C.4).

Phytotoxicity was noted on the treated trees (necrotic spots on leaves), but no damage was noted on the fruits. Common cultural practices were used to maintain plants, and the weather conditions and maintenance chemicals and fertilizer used in this study did not have a notable impact on the residue data.

TABLE C.1. Summary of Method Validation and Concurrent Recoveries of Endothall from Apple.

Matrix	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean ± Std. Dev. (%)
Method Validation				
Fruit	0.05	3	91, 93, 93	92 ± 1
	0.5	3	76, 75, 74	75 ± 1
	5.0	3	92, 104, 94	97 ± 6
	Total	**9**	**74-104**	**88 ± 10**
Concurrent Recoveries				
Fruit	0.05	2	75, 102	89
	0.5	1	77	77
	1.0	1	95	95
	Total	**4**	**75-102**	**87 ± 13**

[1] Standard deviations are calculated for data sets having ≥3 values.

TABLE C.2. Summary of Storage Conditions.			
Matrix	Storage Temperature (°C)	Actual Storage Duration (days)[1]	Interval of Demonstrated Storage Stability (days)[2]
Apple	≤-18	230	467

[1] Interval from harvest to extraction for analysis. Extracts were stored up to 6 days prior to analysis.
[2] Endothall is stable in frozen tomatoes for up to 467 days (47520719.der under review).

TABLE C.3. Residue Data from Apple Field Trials with Endothall Monoalkylamine Salt (SC/L).								
Trial ID (City, State; Year)	Zone	Variety	Matrix	Total Rate		PHI (days)	Residues (ppm)[1, 3]	
				ppm	lb ae/A			
North Rose, NY 2006 NY$29	I	Empire	Fruit	5.0	6.79	0	(0.031)	(0.047)
Ephrata, WA 2006 WA$16	11	Braeburn	Fruit	5.0	6.64	0	ND[4]	(0.043)

[1] The rate is expressed both in terms of the concentration in the irrigation water (ppm) and the total amount (lb ae/A) applied.
[2] Expressed in acid equivalents. The LOQ is 0.05 ppm and the LOD was estimated to be 0.0025 ppm. Values <LOQ but ≥LOD are listed in parentheses.
[3] The two results for each field trial represent two samples taken from a single plot, not two plots.
[4] None Detected at LOD

TABLE C.4. Summary of Residue Data from Pome Fruit Field Trials with Endothall Monoamine Salt (SC/L).									
Commodity	Total Applic. Rate[1]	PHI (days)	Residue Levels (ppm)[2]						
			n	Min.	Max.	HAFT[3]	Median (STMdR)	Mean (STMR)	Std. Dev.
Apple	5 ppm (6.64-6.79)	0	2	0.039	0.043	0.043	0.041	0.041	0.0028

[1] The value in parentheses is the total application rate in terms of lb ae/A.
[2] Residues are expressed in terms of the free acid. The LOQ is 0.05 ppm. For all values reported ≤LOQ, the LOQ was used for all calculations.
[3] HAFT = Highest Average Field Trial.

D. CONCLUSION

The available field trial data are adequate and support the use of endothall-treated water for irrigation of apple trees. The data support the use of endothall in irrigation water at a concentration of 5 ppm (ae), with no more that six applications per season. And a minimum 7-day interval between applications to the water. Residues in the apples represent a 0-day PHI.

E. REFERENCES

None

F. DOCUMENT TRACKING

RDI: David Soderberg (5 June 2009); William Donovan (5 June 2009)
Petition Number: 8E7419
DP#: 356315
PC Code: 038901 and 038905

Template Version June 2005

Primary Evaluator	David Soderberg, Chemist, RABV, HED	Date: 5 June 2009
Approved by	William Donovan, Senior Scientist, RABV, HED	Date: 5 June 2009

This DER was originally prepared under contract by Dynamac Corporation (1910 Sedwick Road, Building 100, Suite B, Durham, NC 27713; submitted 3/27/2009). The DER has been reviewed by the Health Effects Division (HED) and revised as needed for clarity, correctness and to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORT:

47520712. Arsenovic, M. (2008) Endothall (Hydrothol 191): Magnitude of the Residue on Nut Tree Group: Lab Project Number: Z9771. Unpublished study prepared by Interregional Research Project No. 4. 211 pages.

EXECUTIVE SUMMARY:

Interregional Research Project No. 4 (IR-4) submitted field trial data reflecting the exposure of tree nut crops to endothall through the use of treated irrigation water. In a pecan and almond field trial conducted during 2006-2007 in Zones 2 and 10, respectively, a 2.0 lb ae/gal soluble concentrate (SC/L) formulation of endothall (monoalkylamine salt) was used to treat the irrigation water at a rate of 5 ppm ae. [In order to avoid the complications of different molecular weights for different salts, endothall concentrations are expressed as the free acid equivalents (ae).] The treated water was applied to the tree nut crops during nut development and maturation as six broadcast foliar applications using overhead sprinklers, at retreatment intervals (RTIs) of 7-8 days. A volume equivalent to ~1 acre inch of water (27,154 gal/A) was applied for each application. Based on the concentration of the endothall and the amount of water applied, the application rates for endothall were equivalent to 1.13-1.17 lb ae/A/application, for a total of 6.80-7.01 lb ae/A/season.

Single control and duplicate treated samples of pecan and almond nutmeats and almond hulls were harvested from the respective tests on the day of the final application (0 days after treatment, DAT), and samples were stored at ≤-18°C for up to 203 days prior to analysis. Adequate storage stability data are available to support the duration and conditions of sample storage.

Residues of endothall (free acid) in/on nutmeat and almond hull samples were determined using an adequate LC/MS/MS method (Method No. KP-242R1). For this method, residues were extracted with water and then derivatized with heptafluoro-*p*-tolylhydrazine (HFTH) in 50% H_3PO_4. The derivatized residues were cleaned up by partitioning into methyl t-butyl ether (MTBE) and elution through an amine solid phase extraction (SPE) cartridge. Residues were then analyzed by LC/MS/MS using external standards for quantitation. Residues are expressed in endothall acid equivalents. The validated limit of quantitation (LOQ) for endothall in/on nutmeats and hulls is 0.05 ppm.

Following six overhead sprinkler applications with irrigation water containing endothall at 5 ppm (6.80-7.01 lb ae/A/season), endothall residues at 0 DAT were <LOQ in/on two samples each of pecan and almond nutmeats. However, residues were detectable at 0.024 ppm in one of the pecan nutmeat samples and at 0.036 and 0.037 ppm in the two almond nutmeat samples. Residues in/on the two almond hull samples were 6.91 and 8.20 ppm. Average endothall residues and the highest average field trial (HAFT) residues were both 0.05 ppm for nutmeats and 7.56 ppm for almond hulls.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the tree nut field trial residue data are classified as scientifically acceptable. Although limited field trials were performed, these applications are expected to be conservative relative to actual inadvertent applications. The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document, DP# 356315.

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported which would have an adverse impact on the validity of the study.

A. BACKGROUND INFORMATION

Endothall [7-oxabicyclo[2,2,1] heptane-2,3-dicarboxylic acid] is a selective contact herbicide, defoliant, desiccant, and aquatic algaecide that belongs to the dicarboxylic acid chemical class. The free acid of endothall (PC Code 038901) and its dipotassium (PC Code 038904) and alkylamine (PC Code 038905) salts are registered primarily as aquatic herbicides for the control a variety of plants in water bodies. This includes irrigation canals, but only with a 7 day holding period. They are also registered for desiccation/ defoliation of alfalfa/clover (grown for seed only), cotton, and potatoes prior to harvest, and for reduction of sucker branch growth in hops. Permanent tolerances are established for the combined residues of endothall and its monomethyl ester at 0.1 ppm in/on cotton seeds, fish, dried hops and potatoes, and at 0.05 ppm in/on rice grain and straw [40 CFR §180.293(a)(1)].

In conjunction with a petition for tolerances on a wide variety of irrigated crops (PP# 8E7419), IR-4 has submitted field trial data reflecting irrigation of tree nut crops with endothall-treated water. The chemical structure and nomenclature of endothall and its monoalkylamine salt are listed in Table A.1. The physicochemical properties of technical grade endothall and its monoalkylamine salt are listed in Table A.2.

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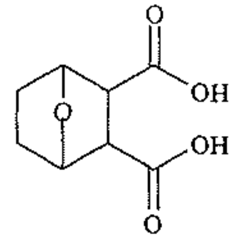
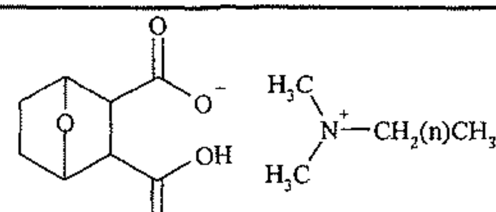
Chemical Structure	
Common name	Endothall
Molecular Formula	$C_8H_{10}O_5$
Molecular Weight	186.16
IUPAC name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid
CAS name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid
CAS #	145-73-3
PC Code	038901
Current Food/Feed Site Registration	Cotton, hops, potato, alfalfa grown for seed
Chemical Structure	 (n = 7-17)
Common name	Endothall, mono-N,N-dimethylalkyl amine salt
Molecular Formula	Not available
Molecular Weight	Average: 422
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CAS name	Not available
CAS #	66330-88-9
PC Code	038905
Current Food/Feed Site Registration	Cotton, hops, potato, alfalfa grown for seed, aquatic uses

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pH	2.7 at 25℃ (1% solution)	D187593, D187590, and D187588, 5/5/93, K. Dockter
Density, bulk density, or specific gravity	0.481 g/cm^3 (bulk) at 25℃	D187593, D187590, and D187588, 5/5/93, K. Dockter
Water solubility at 25℃	109.8 g/L 13.1 g/100 mL in water, pH 5 12.7 g/100 mL in water, pH 7 12.5 g/100 mL in water, pH 9	D166798, 7/2/92, K. Dockter D207011, 9/30/94, F. Toghrol
Solvent solubility at 25℃	3.4 g/100 mL in acetonitrile 2.4 g/100 mL in n-octanol 16.0 g/100 mL in tetrahydrofuran	D207011, 9/30/94, F. Toghrol
Vapor pressure	3.92 x 10^{-5} mm Hg at 24.3℃	D166798, 7/2/92, K. Dockter

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Octanol/water partition coefficient	Not applicable to endothall acid	D166798, 7/2/92, K. Dockter
UV/visible absorption spectrum	Not available	
Endothall, mono-N,N-dimethylalkyl amine salt		
Boiling point	Not available	
pH	5.2 at 25℃ (1% solution)	D187593, D187590, and D187588, 5/5/93, K. Dockter
Density, bulk density, or specific gravity	1.028 g/mL at 25℃	D187593, D187590, and D187588, 5/5/93, K. Dockter
Water solubility at 25℃	≥49.2 g/100mL in water, pH 5 ≥51.6 g/100 mL in water, pH 7 ≥49.8 g/100 mL in water, pH 9	D210814, 8/9/95, S. Knizner
Solvent solubility at 25℃	≥102.5 g/100mL in acetonitrile ≥95.4 g/100 mL in n-octanol ≥104.3 g/100 mL in tetrahydrofuran	D210814, 8/9/95, S. Knizner
Vapor pressure	2.09 x 10^{-5} mm Hg at 25℃ (calculated; mixed mono- and dialkylamine (C8-C20))	D206344, 9/22/94, F. Toghrol
Dissociation constant, pK_a	4.24 for Step 1 and 6.07 for Step 2 at 20℃ for mixed mono- and dialkylamine (C8-C20) in acidified ethanol/water; dissociation complete □17 minutes (1.7 x 10^3 μmho) at 25℃	D198885, 4/7/94, F. Toghrol
Octanol/water partition coefficient	K_{OW} 2.097 at concentrations of 8.9 x 10^{-3} M and 8.9 x 10^{-4} M, at 25℃	D209995, 1/20/95, L. Edwards
UV/visible absorption spectrum	Not available	

B. EXPERIMENTAL DESIGN

B.1. Study Site Information

Field trials were conducted on pecans and almonds in Zones 2 and 10, respectively, during 2006-2007 (Table B.1.1). The irrigation water used in each test was treated with endothall (2.0 lb ae/gal SC monoalkylamine salt) at a concentration of ~5 ppm, acid equivalent. The treated water was applied to each crop during nut development and maturation as six broadcast foliar applications using overhead sprinklers, at RTIs of 7-8 days. A volume equivalent to ~1 acre inch of water (~27,154 gal/A) was applied for each application. Based on the concentration of the endothall and the amount of water applied, application rates for endothall were equivalent to 1.13-1.17 lb ae/A/application, for a total of 6.80-7.01 lb ae/A/season (Table B.1.3). These applications are expected to be conservative relative to actual applications.

TABLE B.1.1. Trial Site Conditions.				
Trial Identification (City, State; Year)	Soil characteristics[1]			
	Type	%OM	pH	CEC (meq/100g)
Irwinville, GA 2006 GA$22	Loamy Sand	1.25	5.3	3.0
Coalinga, CA 2007 CA$40	Silty Clay	1.5	7.0	27.7

[1]These parameters are optional except in cases where their value affects the use pattern for the chemical.

TABLE B.1.2. Water Characterization.

Study site	Water characteristics				
	Type	Hardness/Satinity	pH	Turbidity	Dissolved OM
Irwinville, GA 2006 GA$22	Well	NR	NR	NR	NR
Coalinga, CA 2007 CA$40	Well	NR	NR	NR	NR

NR = Not reported.

The actual temperature recordings and rainfall were typical for each site and no unusual weather conditions were reported. No additional irrigation was reported during the study period. The tests were conducted according to normal agricultural practices for the regions, and information was provided on maintenance pesticides and fertilizers used at each site. No information was provided on the characteristics of the water used for irrigation, other than the source (Table B.1.2).

TABLE B.1.3. Study Use Pattern.

Location (City, State; Year) Trial ID	End-Use Product	Application Information					
		Method; Timing	Concen. [1]	Volume (gal/A) [2]	Single Rate (lb ae/A) [3]	RTI [4] (days)	Total Rate (lb ae/A) [3]
Pecan							
Irwinville, GA 2006 GA$22	2.0 lb/gal SC	Six broadcast foliar application during nut development using overhead sprinklers.	5.0	27,853-28,178	1.16-1.17	7	7.01
Almond							
Coalinga, CA 2007 CA$40	2.0 lb/gal SC	Six broadcast foliar application during nut development using overhead sprinklers.	5.0	27,150	1.13	7-8	6.80

1 The concentration of endothall (in acid equivalents) in the irrigation water. No adjuvants were included in the irrigation water.
2 The target irrigation rate was 1 acre inch of water or 27,154 gal/A.
3 The equivalent field use rates were calculated by the reviewer based on the concentration of the endothall (ae), the application volume and plot size.
4 RTI = Retreatment Interval.

TABLE B.1.3. Trial Numbers and Geographical Locations.

NAFTA Growing Zones[2]	Pecan			Almond		
	Submitted	Requested [1]		Submitted	Requested [1]	
		Canada	U.S.		Canada	U.S.
1	--	--	--	--	--	--
2	1	--	--	--	--	--
3	--	--	--	--	--	--
4	--	--	--	--	--	--
5	--	--	--	--	--	--
6	--	--	--	--	--	--
7	--	--	--	--	--	--
8	--	--	--	--	--	--
9	--	--	--	--	--	--
10	--	--	--	1	--	5
11	--	--	--	--	--	--
12	--	--	--	--	--	--
13	--	--	--	--	--	--
Total	1	--	5	1	--	5

[1] Based on EPA OPPTS Guideline 860.1500.
[2] Zones 1A, 5A and B, 7A and 14-20 were not included as the use is for U.S. only.

B.2. Sample Handling and Preparation

Pecans and almonds were harvested at 0 DAT (after the sixth application). Duplicate control and treated samples (≥2 lbs/sample) were collected from each test and placed in frozen storage at each test facility within 3 hours. Samples were stored frozen at the field sites for 38-47 days. Samples were then shipped by freezer truck to the analytical laboratory, United Phosphorus, Inc. (King of Prussia, PA), and stored at ≤-18EC until analysis.

B.3. Analytical Methodology

Residues of endothall (free acid) in/on nutmeats and almond hulls were determined using a LC/MS/MS method (Method No. KP-242R1) entitled "Analytical Method for Determination of Endothall in Crops", issued 5/4/2007.

For this method, residues were extracted twice by homogenization with water followed by centrifugation and filtering. Residues were then derivatized with HFTH in 50% H_3PO_4 at 100-120°C for 90 minutes. After cooling, the derivatized residues were partitioned into MTBE, evaporated to dryness, and reconstituted in hexane:MTBE (1:1 v:v). Residues were then cleaned using an amine SPE cartridge eluted with methanol:MTBE (1:4). Residues were analyzed by LC/MS/MS using external standards. The m/z 397→166 ion transition was used for quantifying residues. Residues are expressed in endothall acid equivalents. The validated LOQ for endothall in/on nutmeats and hulls is 0.05 ppm. An LOD of 0.00001 ppm was reported; however, this value was the instrument LOD, rather than the LOD of residue in a control matrix.

The above method was validated prior to and in conjunction with the analysis of the field trial samples. Control samples of pecan and almond nutmeats were fortified with endothall at 0.05-5.0 ppm for method validation. For concurrent recoveries, control samples of nutmeats were fortified with endothall at 0.05 and 0.50 ppm and control samples of almond hulls were fortified at 0.05 and 2.0 ppm.

C. RESULTS AND DISCUSSION

The LC/MS/MS method used for determining residues of endothall in/on nutmeats and hulls was adequately validated prior to and in conjunction with the analysis of field trial samples. The average method validation recovery was 75% with a standard deviation of 3% for pecan nutmeat and 77% with a standard deviation of 5% for almond nutmeats (Table C.1). The average concurrent recovery was 79% for pecan nutmeat, 76% for almond nutmeat and 83% for almond hulls. Apparent residues of endothall were <LOQ in/on all control samples. Adequate sample calculations and example chromatograms were provided, and the fortification levels used for the method recoveries were similar in magnitude to the measured residue levels.

Pecan nutmeat, almond nutmeat and almond hull samples were stored at <-18°C for up to 203, 90 and 96 days, respectively, prior to analysis (Table C.2). Adequate storage stability data are available indicating that endothall is stable under frozen storage conditions for up to 315 days in soybean seeds and 466 days in corn grain (47520719.der under review). These data will support the storage durations and conditions for the current field trials.

Following six overhead sprinkler applications with irrigation water containing endothall at 5 ppm (6.80-7.01 lb ae/A/season), endothall residues at 0 DAT were <LOQ in/on all 4 samples of pecan and almond nutmeats (Table C.3). However, endothall was detectable at 0.024 ppm in one of the pecan nutmeat samples and at 0.036 and 0.037 ppm in the two almond nutmeat samples. Residues in/on the two almond hull samples were 6.91 and 8.20 ppm. Average endothall residues were 0.05 ppm for nutmeats and 7.56 ppm for almond hulls (Table C.4). The HAFT residues were 0.05 ppm for nutmeats and 7.56 ppm for hulls.

No phytotoxicity was reported on the treated crops. Common cultural practices were used to maintain plants, and the weather conditions and maintenance chemicals and fertilizer used in this study did not have a notable impact on the residue data.

TABLE C.1. Summary of Method Validation and Concurrent Recoveries of Endothall from Tree Nuts

Matrix	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean ± Std. Dev. (%)
Method Validation				
Pecan Nutmeat	0.05	3	79, 74, 80	78 ± 4
	0.5	3	74, 71, 71	72 ± 2
	5.0	3	74, 75, 74	74 ± 1
	Total	9	**71-81**	**75 ± 3**
Almond Nutmeat	0.05	3	82, 75, 77	78 ±4
	0.5	3	88, 76, 73	79 ±8
	5.0	3	75, 73, 74	74 ± 1
	Total	9	73-88	77 ± 5
Concurrent Recoveries				
Pecan Nutmeat	0.05	1	79	79
	0.5	1	78	
Almond Nutmeat	0.05	1	74	76
	0.5	1	78	
Almond Hulls	0.05	1	87	83
	2.0	1	78	

[1] Standard deviations are calculated for data sets having ≥3 values.

TABLE C.2. Summary of Storage Conditions.

Matrix	Storage Temperature (°C)	Actual Storage Duration (days)[1]	Interval of Demonstrated Storage Stability (days) [2]
Pecan nutmeat	≤-18	203	soybean – 315 corn grain - 466
Almond nutmeat		90	
Almond hull		96	

[1] Interval from harvest to extraction for analysis. Extracts were stored up to 1 day prior to analysis.
[2] Endothall is stable under frozen storage conditions for up to 315 days in soybean seeds and 466 days in corn grain (47520719.der under review).

TABLE C.3. Residue Data from Tree Nut Field Trials with Endothall Monoalkylamine Salt (SC/L).

Trial ID (City, State; Year)	Zone	Crop; Variety	Matrix	Total Rate [1]		PHI (days)	Residues (ppm) [2, 3]	
				ppm	lb ae/A			
Irwinville, GA 2006 GA$22	2	Pecan; summer	Nutmeat	5.0	7.01	0	ND[4]	(0.024)
Coalinga, CA 2007 CA$40	10	Almond; nonpariel	Nutmeat	5.0	6.80	0	(0.036)	(0.037)
			Hulls				6.91	8.20

[1] The rate is expressed both in terms of the concentration in the irrigation water (ppm) and the total amount (lb ae/A) applied.
[2] Expressed in acid equivalents. The LOQ is 0.05 ppm. Values <LOQ but ≥LOD are listed in parentheses.
[3] The two results for each field trial represent two samples taken from a single plot, not two plots.
[4] None detected at LOD

TABLE C.4. Summary of Residue Data from Tree Nut Field Trials with Endothall Monoalkylamine Salt (SC/L). FIX

Commodity	Total Applic. Rate [1]	PHI (days)	Residue Levels (ppm) [2]						
			n	Min.	Max.	HAFT [3]	Median (STMdR)	Mean (STMR)	Std. Dev.
Pecan, nutmeat	5 ppm (7.01)	0	1	0.24	024	0.024	0.024	0.024	N/A
Almond, nutmeat	5 ppm (6.80)	0	1	0.037	0.037	<0.037	0.037	0.037	N/A
Almond, hulls		0	1	7.56	7.56	7.56	7.56	7.56	N/A

[1] The value in parentheses is the total application rate in terms of lb ae/A.
[2] Residues are expressed in terms of the free acid. The LOQ is 0.05 ppm. For all values reported ≤LOQ, the LOQ was used for all calculations.
[3] HAFT = Highest Average Field Trial.

D. CONCLUSION

The available field trial data are adequate and support the use of endothall-treated water for irrigation of tree nut crops. The data support the use of endothall in irrigation water at a concentration of 5 ppm (ae), with no more that six applications per season and a minimum 7-day interval between applications to the water. Residues on the nut crops were determined at a 0-day PHI.

E. REFERENCES

None

F. DOCUMENT TRACKING

RDI: David Soderberg (5 June 2009); William Donovan (5 June 2009)
Petition Number: 8E7419
DP#: 356315
PC Code: 038901 and 038905

Template Version June 2005

Primary Evaluator [signature] Date: 5 June 2009
David Soderberg, Chemist, RABV, HED

Approved by [signature] Date: 5 June 2009
William Donovan, Senior Scientist, RABV, HED

This DER was originally prepared under contract by Dynamac Corporation (1910 Sedwick Road, Building 100, Suite B, Durham, NC 27713; submitted 3/31/2009). The DER has been reviewed by the Health Effects Division (HED) and revised as needed for clarity, correctness and to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORT:

47520713. Arsenovic, M. (2008) Endothall (Hydrothol 191): Magnitude of the Residue on Grain Cereal Group (Except Rice): Lab Project Number: Z9768. Unpublished study prepared by Interregional Research Project No. 4. 590 pages.

EXECUTIVE SUMMARY:

Interregional Research Project No. 4 (IR-4) submitted field trial data reflecting the exposure of representative cereal grain crops to endothall through the use of treated irrigation water. A total of 13 field trials were conducted during the 2006 and 2007 growing seasons in Zones 1, 2, 5, 6, 7, and 11, including two trials on sweet corn, four trials on field corn, three trials on sorghum, and four trials on wheat (3 winter wheat and 1 spring wheat). In each test, the 2.0 lb ae/gal soluble concentrate (SC/L) formulation of endothall (monoalkylamine salt) was used to treat the irrigation water at a rate of 5 ppm ae. [In order to avoid the complications of different molecular weights for different salts, endothall concentrations are expressed as the free acid equivalents (ae).] The treated water was applied to each crop during seed head formation and development as six broadcast foliar applications using overhead sprinklers, at retreatment intervals (RTIs) of 6-9 days. A volume equivalent to ~1 acre inch of water (27,154 gal/A) was applied for each application. Based on the concentration of the endothall in the irrigation water and the amount of water applied, the overall application rates for endothall were equivalent to 1.10-1.25 lb ae/A/application, for a total of 6.58-7.10 lb ae/A/season. As samples of field corn forage, sorghum forage, and wheat forage and hay were harvested after only 2 or 3 applications, the total application rates for these commodities was 2.19-3.39 lb ae/A.

Duplicate control and treated samples of each commodity were harvested from the respective tests. Samples of field corn forage, sorghum forage and wheat forage and hay were harvested 0 days after the second or third application (0 DAT). Samples of sweet corn forage, kernels plus cob with husks removed (K+CWHR) and stover, field corn grain and stover, sorghum grain and stover, and wheat grain and straw were harvested following the sixth application at 0 DAT (or at 1 DAT in one wheat test). Samples of all cereal grain commodities were stored at ≤-18°C for up to 238 days prior to analysis. Adequate storage stability data are available to support the duration and conditions of sample storage.

Residues of endothall (free acid) in/on cereal grain commodities were determined using an adequate LC/MS/MS method (Method No. KP-242R1). For this method, residues were extracted with water and then derivatized with heptafluoro-*p*-tolylhydrazine (HFTH) in 50% H_3PO_4. The derivatized residues were cleaned up by partitioning into methyl t-butyl ether (MTBE) and elution through an amine solid phase extraction (SPE) cartridge. Residues were then analyzed by LC/MS/MS using external standards for quantitation. Residues are expressed in endothall acid equivalents. The validated limit of quantitation (LOQ) for endothall in/on each cereal grain commodity is 0.05 ppm.

In the sweet corn field trials, endothall residues at 0 DAT were <0.05-0.17 ppm in/on 4 samples of K+CWHR, 0.52-1.28 ppm in/on 4 samples of forage without ears, 0.40-1.06 ppm in/on 4 samples of forage with ears, and 0.58-5.06 ppm in/on 4 samples of stover with ears. Average endothall residues were 0.11 ppm for K+CWHR, 0.91 ppm for forage without ears, 0.71 ppm for forage with ears, and 2.76 ppm for stover with ears. The HAFT residues were 0.17 ppm in/on K+CWHR, 1.23 ppm in/on forage without ears, 0.97 ppm in/on forage with ears, and 4.88 ppm in/on stover with ears.

In the field corn field trials, endothall residues at 0 DAT were 0.21-0.42 ppm in/on 8 samples of forage harvested after only 2 or 3 applications (2.26-3.38 lb ae/A). Following all six applications (6.75-7.10 lb ae/A), endothall residues at 0 DAT were <0.05 ppm in/on 8 samples of grain and 1.07-3.48 ppm in/on 8 samples of stover. Average endothall residues were 0.33 ppm for forage, <0.05 ppm for grain, and 2.08 ppm for stover. The HAFT residues were 0.385 ppm in/on forage, <0.05 ppm in/on grain, and 3.19 ppm in/on stover.

In the sorghum field trials, endothall residues at 0 DAT were 0.29-3.05 ppm in/on 6 samples of forage harvested after only 2 or 3 applications (2.26-3.38 lb ae/A). Following all six applications (6.77 lb ae/A), endothall residues at 0 DAT were 0.49-1.41 ppm in/on 6 samples of grain and 0.81-7.19 ppm in/on 6 samples of stover. Average endothall residues were 1.26 ppm for forage, 1.00 ppm for grain, and 2.91 ppm for stover. The HAFT residues were 2.67 ppm in/on forage, 1.21 ppm in/on grain, and 4.90 ppm in/on stover.

In the wheat field trials, endothall residues at 0 DAT were 0.63-2.27 ppm in/on 8 samples of forage and 1.00-3.09 ppm in/on 8 samples of hay harvested after only 2 or 3 applications (2.19-3.39 lb ae/A). Following all six applications (6.58-6.77 lb ae/A), endothall residues at 0 or 1 DAT were 0.20-2.01 ppm in/on 8 samples of grain and 0.61-2.76 ppm in/on 8 samples of straw. Average endothall residues were 1.15 ppm for forage, 1.94 ppm for hay, 0.71 ppm for grain, and 1.83 ppm for straw. The HAFT residues were 2.13 ppm in/on forage, 3.09 ppm in/on hay, 1.91 ppm in/on grain, and 2.74 ppm in/on straw. Residue decline data were not provided in any field trials.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in this study, the residue data on sweet corn forage, K+CWHR and stover, field corn grain and stover, sorghum grain and stover, and wheat grain and straw are classified as scientifically acceptable. However, the residue data on field corn forage, sorghum forage, and wheat forage and hay did not receive all six possible applications prior to harvest, and therefore may not be conservative. The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document, DP# 356315.

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported which would have an adverse impact on the validity of the study.

A. BACKGROUND INFORMATION

Endothall [7-oxabicyclo[2,2,1] heptane-2,3-dicarboxylic acid] is a selective contact herbicide, defoliant, desiccant, and aquatic algicide that belongs to the dicarboxylic acid chemical class. The free acid of endothall (PC Code 038901) and its dipotassium (PC Code 038904) and alkylamine (PC Code 038905) salts are registered primarily as aquatic herbicides for the control a variety of plants in water bodies. This includes irrigation canals, but only with a 7 day holding period. They are also registered for desiccation/ defoliation of alfalfa/clover (grown for seed only), cotton, and potatoes prior to harvest, and for reduction of sucker branch growth in hops. Permanent tolerances are established for the combined residues of endothall and its monomethyl ester at 0.1 ppm in/on cotton seeds, fish, dried hops and potatoes, and at 0.05 ppm in/on rice grain and straw [40 CFR §180.293(a)(1)].

In conjunction with a petition for tolerances on a wide variety of irrigated crops (PP# 8E7419), IR-4 has submitted field trial data reflecting irrigation of representative cereal grains with endothall-treated water. The chemical structure and nomenclature of endothall and its monoalkylamine salt are listed in Table A.1. The physicochemical properties of technical grade endothall and its monoalkylamine salt are listed in Table A.2.

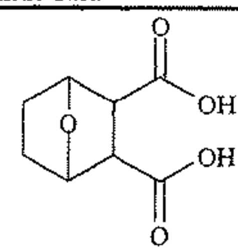
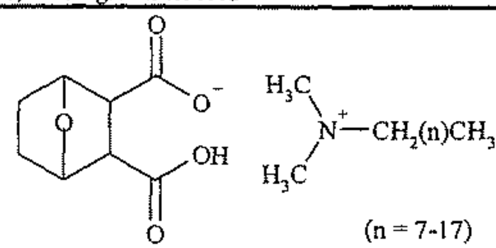
Table A.1. Nomenclature of Endothall and its Monoalkylamine Salt.	
Chemical Structure	
Common name	Endothall
Molecular Formula	$C_8H_{10}O_5$
Molecular Weight	186.16
IUPAC name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid
CAS name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid
CAS #	145-73-3
PC Code	038901
Current Food/Feed Site Registration	Cotton, hops, potato, alfalfa grown for seed
Chemical Structure	 (n = 7-17)
Common name	Endothall, mono-N,N-dimethylalkyl amine salt
Molecular Formula	Not available
Molecular Weight	Average: 422
IUPAC name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid, compound with N,N-dimethylcocoamine
CAS name	Not available
CAS #	66330-88-9
PC Code	038905
Current Food/Feed Site Registration	Cotton, hops, potato, alfalfa grown for seed, aquatic uses

Table A.2. Physicochemical Properties of Endothall and Its Monoalkylamine Salt.		
Parameter	Value	Reference
Endothall (acid)		
Melting point	108-110℃	D187593, D187590, and D187588, 5/5/93, K. Dockter
pH	2.7 at 25℃ (1% solution)	D187593, D187590, and D187588, 5/5/93, K. Dockter
Density, bulk density, or specific gravity	0.481 g/cm^3 (bulk) at 25℃	D187593, D187590, and D187588, 5/5/93, K. Dockter
Water solubility at 25℃	109.8 g/L 13.1 g/100 mL in water, pH 5 12.7 g/100 mL in water, pH 7 12.5 g/100 mL in water, pH 9	D166798, 7/2/92, K. Dockter D207011, 9/30/94, F. Toghrol
Solvent solubility at 25℃	3.4 g/100 mL in acetonitrile 2.4 g/100 mL in n-octanol 16.0 g/100 mL in tetrahydrofuran	D207011, 9/30/94, F. Toghrol
Vapor pressure	3.92×10^{-5} mm Hg at 24.3℃	D166798, 7/2/92, K. Dockter
Dissociation constant, pK_a	4.32 for Step 1 and 6.22 for Step 2 at 20℃ (0.2% solution in 20% basic ethanol); dissociation rate $1.8\text{-}2.3 \times 10^3$ µmho within 3-5 minutes at □25℃, by conductivity meter	D188708, 5/3/93, K. Dockter
Octanol/water partition coefficient	Not applicable to endothall acid	D166798, 7/2/92, K. Dockter
UV/visible absorption spectrum	Not available	
Endothall, mono-N,N-dimethylalkyl amine salt		
Boiling point	Not available	
pH	5.2 at 25℃ (1% solution)	D187593, D187590, and D187588, 5/5/93, K. Dockter
Density, bulk density, or specific gravity	1.028 g/mL at 25℃	D187593, D187590, and D187588, 5/5/93, K. Dockter
Water solubility at 25℃	≥49.2 g/100mL in water, pH 5 ≥51.6 g/100 mL in water, pH 7 ≥49.8 g/100 mL in water, pH 9	D210814, 8/9/95, S. Knizner
Solvent solubility at 25℃	≥102.5 g/100mL in acetonitrile ≥95.4 g/100 mL in n-octanol ≥104.3 g/100 mL in tetrahydrofuran	D210814, 8/9/95, S. Knizner
Vapor pressure	2.09×10^{-5} mm Hg at 25℃ (calculated; mixed mono- and dialkylamine (C8-C20))	D206344, 9/22/94, F. Toghrol
Dissociation constant, pK_a	4.24 for Step 1 and 6.07 for Step 2 at 20℃ for mixed mono- and dialkylamine (C8-C20) in acidified ethanol/water; dissociation complete □17 minutes (1.7×10^3 µmho) at 25℃	D198885, 4/7/94, F. Toghrol
Octanol/water partition coefficient	K_{OW} 2.097 at concentrations of 8.9×10^{-3} M and 8.9×10^{-4} M, at 25℃	D209995, 1/20/95, L. Edwards
UV/visible absorption spectrum	Not available	

B. EXPERIMENTAL DESIGN

B.1. Study Site Information

A total of 13 field trials were conducted on representative cereal grains in Zones 1, 2, 5, 6, 7, and 11 during the 2006 and 2007 growing seasons (Table B.1.1), including two trials on sweet corn, four trials on field corn, three trials on sorghum, and four trials on wheat (3 winter wheat and 1 spring wheat). In each test, the irrigation water was treated with endothall (2.0 lb ae/gal SC monoalkylamine salt) at a concentration of ~5 ppm, acid equivalent. The treated water was applied to each crop from seed head development through grain maturation as six broadcast foliar applications using overhead sprinklers, at RTIs of 6-9 days. A volume equivalent to ~1 acre inch of water (~27,154 gal/A) was typically applied for each application. Based on the concentration of the endothall and the amount of water applied, the overall application rates for endothall were equivalent to 1.10-1.25 lb ae/A/application, for a total of 6.58-7.10 lb ae/A/season (Table B.1.3).

As samples of field corn forage, sorghum forage, and wheat forage and hay were harvested after only 2 or 3 applications, the total application rates for these commodities was 2.19-3.39 lb ae/A.

TABLE B.1.1. *Trial Site Conditions.*

Trial Identification (City, State; Year)	Soil characteristics[1]			
	Type	%OM	pH	CEC (meq/100g)
Sweet Corn				
Sodus, NY 2006 NY$17	Gravelly Loam	3.2	6.4	13.4
Campbell, MN 2007 MN$10	Clay Loam	4.8	6.7	30.2
Field Corn				
Baptistown, NJ 2006 NJ$18	Loam	2.3	6.7	9.1
Sparta, IL 2007 IL$09	Silt	2.5	6.9	10
Richland, IA 2007 IA$06	Silty Clay Loam	4.88	6.53	23.7
Centerville, SD 2007 SD$05	Sandy Loam	2.1	7.4	12.89
Sorghum				
Sparta, IL 2007 IL$08	Silt	2.5	6.9	10.9
Richland, IA 2007 IA$07	Silty Clay Loam	3.68	6.20	22.5
Larned, KS 2007 KS$03	Sandy Clay Loam	0.7	5.7	6
Wheat				
Ephrata, WA 2007 WA$20	Loamy Sand	0.8	7.7	11.7
Bernard, TX 2007 TX$19	Sandy Clay Loam	0.3	6.9	7.1
St, Johns, KS 2007 KS$21	Sand	0.7	7.7	3.8
Velva, ND 2007 ND$04	Loam	3.2	5.6	17.8

[1]These parameters are optional except in cases where their value affects the use pattern for the chemical.

TABLE B.1.1.2 Water Characterization.

Study site	Water characteristics				
	Type	Hardness/Salinity	pH	Turbidity	Dissolved OM
Sodus, NY 2006 NY$17	Well	NR	NR	NR	NR
Campbell. MN 2007 MN$10	Well	NR	NR	NR	NR
Baptistown, NJ 2006 NJ$18	Well	NR	NR	NR	NR
Sparta, IL 2007 IL$09	Well	NR	NR	NR	NR
Richland, IA 2007 IA$06	Well	NR	NR	NR	NR
Centerville, SD 2007 SD$05	Well	NR	NR	NR	NR
Sparta, IL 2007 IL$08	Well	NR	NR	NR	NR
Richland, IA 2007 IA$07	Well	NR	NR	NR	NR
Larned, KS 2007 KS$03	Well	NR	NR	NR	NR
Ephrata, WA 2007 WA$20	Well	NR	NR	NR	NR
Bernard, TX 2007 TX$19	Well	NR	NR	NR	NR
St, Johns, KS 2007 KS$21	Well	NR	NR	NR	NR
Velva, ND 2007 ND$04	Well	NR	NR	NR	NR

NR = not reported.

The actual temperature recordings and rainfall were typical for each site and no unusual weather conditions were reported. No additional irrigation was reported during the study period. The tests were conducted according to normal agricultural practices for the regions, and information was provided on maintenance pesticides and fertilizers used at each site. No information was provided on the characteristics of the water used for irrigation, other than the source (Table B.1.2).

TABLE B.1.2. Study Use Pattern.

Location (City, State; Year) Trial ID	End-Use Product	Application Information					
		Method [1]; Timing	Concen. [2] (ppm)	Volume (gal/A) [3]	Single Rate (lb ae/A) [4]	RTI [5] (days)	Total Rate (lb ae/A) [4]
Sweet Corn							
Sodus, NY 2006 NY$17	2.0 lb ae/gal SC/L	Six broadcast foliar applications from 5-6 true leaves to mature ears	5.0	27,140	1.13	6-9	6.75
Campbell. MN 2007 MN$10	2.0 lb ae/gal SC/L	Six broadcast foliar applications from V9 or V10 to milk stage	5.0	27,696-27,720	1.15	6-8	6.91

TABLE B.1.2. Study Use Pattern.

Location (City, State; Year) Trial ID	End-Use Product	Application Information					
		Method [1]; Timing	Concen. [2] (ppm)	Volume (gal/A) [3]	Single Rate (lb ae/A) [4]	RTI [5] (days)	Total Rate (lb ae/A) [4]
Field Corn							
Baptistown, NJ 2006 NJ$18	2.0 lb ae/gal SC/L	Six broadcast foliar applications from milk stage (R3) to maturity (R6)	5.0	27,154	1.13	7	6.75
Sparta, IL 2007 IL$09	2.0 lb ae/gal SC/L	Six broadcast foliar applications from 13-14 true leaves	5.0	27,154	1.13	6-8	6.77
Richland, IA 2007 IA$06	2.0 lb ae/gal SC/L	Six broadcast foliar applications from late dough (BBCH 85) to maturity (BBCH 89)	5.0	27,154	1.13	6-8	6.77
Centerville, SD 2007 SD$05	2.0 lb ae/gal SC/L	Six broadcast foliar applications from dough stage to maturity	5.0	27,078-30,202	1.12-1.25	6-7	7.10
Sorghum							
Sparta, IL 2007 IL$08	2.0 lb ae/gal SC/L	Six broadcast foliar applications during seed head development	5.0	27,154	1.13	6-8	6.77
Richland, IA 2007 IA$07	2.0 lb ae/gal SC/L	Six broadcast foliar applications from mid-milk (BBCH 75) to maturity (BBCH 89)	5.0	27,154	1.13	7	6.77
Larned, KS 2007 KS$03	2.0 lb ae/gal SC/L	Six broadcast foliar applications from early dough (BBCH 83) to maturity (BBCH 89)	5.0	27,161	1.13	6-7	6.77
Wheat							
Ephrata, WA 2007 WA$20	2.0 lb ae/gal SC/L	Six broadcast foliar applications from soft dough to maturity	5.0	26,715	1.11	6-8	6.64
Bernard, TX 2007 TX$19	2.0 lb ae/gal SC/L	Six broadcast foliar applications from end of flowering (BBCH 69) to maturity (BBCH 89)	5.0	26,926-26,938	1.12	6-8	6.71
St, Johns, KS 2007 KS$21	2.0 lb ae/gal SC/L	Six broadcast foliar applications from end of heading (BBCH 59) to maturity (BBCH 87)	5.0	27,160	1.13	6-8	6.77
Velva, ND 2007 ND$04	2.0 lb ae/gal SC/L	Six broadcast foliar applications from heading to maturity	5.0	26,365	1.10	7	6.58

1 All applications were made using overhead sprinkler systems.
2 The concentration of endothall (in acid equivalents) in the irrigation water. No adjuvants were included in the irrigation water.
3 The target irrigation rate was 1 acre inch of water or 27,154 gal/A.
4 The equivalent field use rates were calculated by the reviewer based on the concentration of the endothall (ae), the application volume and plot size.
5 RTI = Retreatment Interval.

TABLE B.1.3. Trial Numbers and Geographical Locations.

NAFTA Growing Zones[2]	Sweet Corn			Field Corn			Sorghum			Wheat		
	Submitted	Requested[1]		Submitted	Requested[1]		Submitted	Requested[1]		Submitted	Requested[1]	
		Canada	U.S.		Canada	U.S.		Canada	U.S.		Canada	U.S.
1	1	--	1	--	--	1	--	--	--	--	--	--
2	--	--	1	1	--	1	--	--	--	--	--	1
3	--	--	1	--	--	--	--	--	--	--	--	--
4	--	--	--	--	--	--	--	--	1	--	--	1
5	1	--	3	3	--	12	2	--	3	1	--	3
6	--	--	--	--	--	1	--	--	2	1	--	1
7	--	--	--	--	--	--	1	--	1	1	--	4
8	--	--	--	--	--	--	--	--	2	--	--	4
9	--	--	--	--	--	--	--	--	--	--	--	--
10	--	--	1	--	--	--	--	--	--	--	--	--
11	--	--	1	--	--	--	--	--	--	1	--	--
12	--	--	1	--	--	--	--	--	--	--	--	--
13	--	--		--	--	--	--	--	--	--	--	--
Total	2	--	9	4	--	15	--	--	9	4	--	15

1 Based on EPA OPPTS Guideline 860.1500. Indicates a 25% reduction for a crop group.
2 Zones 1A, 5A and B, 7A and 14-20 were not included das the use is for U.S. only.

B.2. Sample Handling and Preparation

Samples of each sweet corn commodity, field corn grain and stover, and sorghum grain and stover were harvested at 0 DAT after the sixth application, and wheat grain and straw were harvested at 0 or 1 DAT after the sixth application. Samples of field corn forage, sorghum forage and wheat forage and hay were harvested 0 days after the second or third application. Duplicate control and treated samples of each commodity ($\geq$1 lb/sample) were collected from the respective tests and placed in frozen storage at each test facility within 2.5 hours. Prior to storage, samples of sweet corn stover were dried for 2-8 days, samples of sorghum stover were dried for 1-2 days, and samples of wheat hay were dried for 1-6 days. The collected samples were stored frozen at the field sites for 7-55 days. Samples were then shipped by ACDS freezer truck to the analytical laboratory, United Phosphorus, Inc. (King of Prussia, PA), and stored frozen ($\leq$-18EC) prior to analysis.

B.3. Analytical Methodology

Residues of endothall (free acid) in/on grain, forage, stover and sweet corn K+CWHR were determined using a LC/MS/MS method (Method No. KP-242R1) entitled "Analytical Method for Determination of Endothall in Crops", issued 5/4/2007.

For this method, residues were extracted twice by homogenization with water followed by centrifugation and filtering. Residues were then derivatized with HFTH in 50% H_3PO_4 at 100-120°C for 90 minutes. After cooling, the derivatized residues were partitioned into MTBE, evaporated to dryness, and reconstituted in hexane:MTBE (1:1 v/v). Residues were then cleaned using an amine SPE cartridge eluted with methanol:MTBE (4:1,v/v). Residues were analyzed by

LC/MS/MS using external standards. The m/z 397→166 ion transition was used for quantifying residues. Residues are expressed in endothall acid equivalents. The validated LOQ for endothall in/on forage and hay is 0.05 ppm. An LOD of 0.00001 ppm was reported; however, this value was the instrument LOD, rather than the LOD of residues in a control matrix.

Control samples of wheat grain and corn grain, forage and forage w/ ears were fortified with endothall at 0.05-5.0 ppm for method validation. For concurrent recoveries, control samples were fortified with endothall at 0.05-4.0 ppm for forage, hay, stover and straw, 0.05-2.0 ppm for grain and K+CWHR.

C. RESULTS AND DISCUSSION

The LC/MS/MS method used for determining residues of endothall in/on cereal grain commodities was adequately validated prior to and in conjunction with the analysis of field trial samples. Average method validation recoveries (±SD) were 88 ± 6% for corn grain, 96 ± 7% for corn forage, 92 ± 5% for corn forage with ears, and 75 ± 3% for wheat grain (Table C.1). Average Concurrent recoveries for each commodity were 75-95% with standard deviations of 4-15%. Apparent residues of endothall were <LOQ in/on control samples of each matrix. Adequate sample calculations and example chromatograms were provided, and the fortification levels used for the method recoveries were similar in magnitude to the measured residue levels.

Samples were stored at <-18°C for up to 238 days prior to analysis (Table C.2). Adequate storage stability data are available indicating that endothall is stable for up to 465-469 days in frozen tomatoes, lettuce, corn grain and sugar beet roots and up to 316 days in frozen soybeans (47520719.der, under review). These stability data will support the storage durations and conditions for the current cereal grain field trials.

In the sweet corn field trials, endothall residues at 0 DAT were <0.05-0.17 ppm in/on 4 samples of K+CWHR, 0.52-1.28 ppm in/on 4 samples of forage without ears, 0.40-1.06 ppm in/on 4 samples of forage with ears, and 0.58-5.06 ppm in/on 4 samples of stover with ears (Table C.3). Average endothall residues were 0.11 ppm for K+CWHR, 0.91 ppm for forage without ears, 0.71 ppm for forage with ears, and 2.76 ppm for stover with ears (Table C.4). The HAFT residues were 0.17 ppm in/on K+CWHR, 1.23 ppm in/on forage without ears, 0.97 ppm in/on forage with ears, and 4.88 ppm in/on stover with ears.

In the field corn field trials, endothall residues at 0 DAT were 0.21-0.42 ppm in/on 8 samples of forage harvested after only 2 or 3 applications (2.26-3.38 lb ae/A). Following all six applications (6.75-7.10 lb ae/A), endothall residues at 0 DAT were <0.05 ppm in/on 8 samples of grain and 1.07-3.48 ppm in/on 8 samples of stover. Average endothall residues were 0.33 ppm for forage, <0.05 ppm for grain, and 2.08 ppm for stover. The HAFT residues were 0.385 ppm in/on forage, <0.05 ppm in/on grain, and 3.19 ppm in/on stover.

In the sorghum field trials, endothall residues at 0 DAT were 0.29-3.05 ppm in/on 6 samples of forage harvested after only 2 or 3 applications (2.26-3.38 lb ae/A). Following all six applications (6.77 lb ae/A), endothall residues at 0 DAT were 0.49-1.41 ppm in/on 6 samples of grain and

0.81-7.19 ppm in/on 6 samples of stover. Average endothall residues were 1.26 ppm for forage, 1.00 ppm for grain, and 2.91 ppm for stover. The HAFT residues were 2.67 ppm in/on forage, 1.21 ppm in/on grain, and 4.90 ppm in/on stover.

In the wheat field trials, endothall residues at 0 DAT were 0.63-2.27 ppm in/on 8 samples of forage and 1.00-3.09 ppm in/on 8 samples of hay harvested after only 2 or 3 applications (2.19-3.39 lb ae/A). Following all six applications (6.58-6.77 lb ae/A), endothall residues at 0 or 1 DAT were 0.20-2.01 ppm in/on 8 samples of grain and 0.61-2.76 ppm in/on 8 samples of straw. Average endothall residues were 1.15 ppm for forage, 1.94 ppm for hay, 0.71 ppm for grain, and 1.83 ppm for straw. The HAFT residues were 2.13 ppm in/on forage, 3.09 ppm in/on hay, 1.91 ppm in/on grain, and 2.74 ppm in/on straw.

No phytotoxicity was reported on any of the cereal grain crops. Common cultural practices were used to maintain plants, and the weather conditions and maintenance chemicals and fertilizer used in this study did not have a notable impact on the residue data.

TABLE C.1. Summary of Method Validation and Concurrent Recoveries of Endothall from Cereal Grains

Crop	Matrix	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean ± Std. Dev. (%)
Method Validation					
Corn	Grain	0.05	3	96, 81, 93	90 ± 8
		0.5	3	80, 92, 90	87 ± 6
		5.0	3	88, 86, 83	86 ± 3
		Total	**9**	**80-96**	**88 ± 6**
	Forage	0.05	3	100, 105, 108	104 ± 4
		0.5	3	96, 93, 88	92 ± 4
		5.0	3	89, 98, 87	91 ± 6
		Total	**9**	**87-108**	**96 ± 7**
	Forage with ears	0.05	3	91, 93, 90	91 ± 2
		0.5	3	87, 93, 90	90 ± 3
		5.0	3	104, 87, 90	94 ± 9
		Total	**9**	**87-104**	**92 ± 5**
Wheat	Grain	0.05	3	75, 76, 73	75 ± 2
		0.5	3	76, 72, 72	73 ± 2
		5.0	3	83, 73, 77	78 ± 5
		Total	9	72-83	75 ± 3

TABLE C.1. Summary of Method Validation and Concurrent Recoveries of Endothall from Cereal Grains

Crop	Matrix	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean ± Std. Dev. (%)
Concurrent Recoveries					
Corn	Forage	0.05	6	71, 97, 80, 74, 108, 70	83 ± 16
		0.5	1	85	85
		1.0	2	82, 75	79 ± 5
		2.0	3	84, 87, 73	81 ± 7
		Total	**12**	**70-108**	**82 ± 11**
	Forage with ears	0.05	2	100, 111	106 ± 8
		1.0	1	90	90
		2.0	1	78	78
		Total	**4**	**78-111**	**95 ± 14**
	Grain	0.05	4	76, 72, 70, 70	72 ± 3
		0.2	2	74, 81	78 ± 5
		0.5	2	78, 70	74 ± 6
		Total	**8**	**70-81**	**74 ± 4**
	K+CWHR	0.05	2	94, 105	100 ± 8
		0.5	1	80	80
		2.0	1	71	71
		Total	**4**	**71-105**	**88 ± 15**
	Stover	0.05	6	76, 77, 88, 110, 81, 81	86 ± 13
		1.0	4	90, 79, 73, 75	79 ± 8
		2.0	1	84	84
		4.0	1	82	82
		Total	**12**	**73-110**	**83 ± 10**
Sorghum	Forage	0.05	3	75, 88, 95	86 ± 10
		0.5	1	75	75
		1.0	1	71	71
		4.0	1	106	106
		Total	**6**	**71-106**	**85 ± 14**
	Grain	0.05	3	81, 72, 77	77 ± 5
		0.5	1	75	75
		1.0	2	80, 72	76 ± 6
		Total	**6**	**72-81**	**76 ± 4**
	Stover	0.05	2	72, 85	79 ± 9
		1.0	2	79, 71	75 ± 6
		Total	**4**	**71-85**	**77± 7**

TABLE C.1. Summary of Method Validation and Concurrent Recoveries of Endothall from Cereal Grains

Crop	Matrix	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean ± Std. Dev. (%)
Wheat	Forage	0.05	4	70, 78, 72, 85	76 ± 7
		1.0	2	80, 74	77 ± 4
		2.0	2	76, 80	78 ± 3
		Total	**8**	**70-85**	**77 ± 5**
	Grain	0.05	4	79, 80, 71, 80	78 ± 4
		0.5	2	71, 70	71 ± 1
		1.0	1	77	77
		2.0	1	72	72
		Total	**8**	**70-80**	**75 ± 4**
	Hay	0.05	4	70, 70, 73, 70	71 ± 2
		0.1	1	74	74
		1.0	1	113	113
		2.0	1	74	74
		4.0	1	73	73
		Total	**8**	**70-113**	**77 ± 15**
	Straw	0.05	4	78, 72, 72, 73	74 ± 3
		2.0	2	72, 72	72
		3.0	1	90	90
		4.0	1	76	76
		Total	**8**	**72-90**	**76 ± 6**

[1] Standard deviations are calculated for data sets having ≥3 values.

TABLE C.2. Summary of Storage Conditions.

Crop	Matrix	Storage Temperature (°C)	Actual Storage Duration (days)[1]	Interval of Demonstrated Storage Stability (days)[2]
Corn	K+CWHR	≤-18	51-238	316-469
	forage		45-237	
	grain		44-139	
	stover		42-236	
Sorghum	forage		69-83	
	grain		51-61	
	stover		54-61	
Wheat	forage		50-113	
	grain		54-86	
	hay		42-104	
	straw		55-85	

[1] Interval from harvest to extraction for analysis. Extracts were stored 0-10 days prior to analysis.
[2] Based on storage stability data from frozen tomatoes, lettuce, corn grain, sugar beet roots, and soybean seeds (47520719.der, under review).

TABLE C.3. Residue Data from Crop Field Trials with Endothall.

Trial ID (City, State; Year)	Zone	Crop; Variety	Matrix	Total Rate [1] ppm	Total Rate [1] (lb ae/A)	PHI (days)	Residues (ppm) [2, 6]	
Sweet Corn								
Sodus, NY 2006 NY$17	1	Sweet corn; Speedy Sweet	K+CWHR	5.0	6.75	0	0.05	<0.05
			Forage (w/o ears)				0.52	0.65
			Forage (w/ears)				0.49	0.40
			Stover (w/ears)				0.69	0.58
Campbell. MN 2007 MN$10	5	Sweet corn: Vitality	K+CWHR	5.0	6.91	0	0.17	0.17
			Forage (w/o ears)				1.18	1.28
			Forage (w/ears)				0.88	1.06
			Stover (w/ears)				4.70	5.06
Field Corn								
Baptistown, NJ 2006 NJ$18	2	Field corn; TA 3892	Forage	5.0	3.38 [4]	0	0.40	0.28
			Grain		6.75		(0.041) [5]	(0.039) [5]
			Stover				3.48	2.89
Sparta, IL 2007 IL$09	5	Field Corn DK61-73	Forage	5.0	6.77	0	0.31	0.34
			Grain				<0.05	<0.05
			Stover				1.56	1.39
Richland, IA 2007 IA$06	5	Field Corn 34A16	Forage	5.0	2.26 [3]	0	0.35	0.42
			Grain		6.77		<0.05	<0.05
			Stover				2.07	2.37
Centerville, SD 2007 SD$05	5	Field Corn DKC 54-46	Forage	5.0	2.40 [3]	0	0.36	0.21
			Grain		7.10		<0.05	<0.05
			Stover				1.07	1.81
Sorghum								
Sparta, IL 2007 IL$08	5	Sorghum Dekalb 44	Forage	5.0	3.38 [4]	0	3.05	2.29
			Grain		6.77		1.41	0.91
			Stover				2.60	7.19
Richland, IA 2007 IA$07	5	Sorghum 85G01	Forage	5.0	3.38 [4]	0	0.96	0.57
			Grain		6.77		0.49	0.80
			Stover				1.11	0.81
Larned, KS 2007 KS$03	7	Sorghum Pioneer 87G57	Forage	5.0	2.26 [3]	0	0.29	0.41
			Grain		6.77		1.23	1.18
			Stover				3.10	2.65
Wheat								
Ephrata, WA 2007 WA$20	11	Winter Wheat; Stevens	Forage	5.0	2.21 [3]	0	0.74	0.63
			Hay				1.00	1.11
			Grain		6.64		0.20	0.25
			Straw				2.20	1.93
Bernard, TX 2007 TX$19	6	Winter wheat; Fannin	Forage	5.0	2.24 [1]	0	1.99	2.27
			Hay				3.09	3.09
			Grain		6.71	1	2.01	1.80
			Straw				2.72	2.76

TABLE C.3. Residue Data from Crop Field Trials with Endothall.

Trial ID (City, State; Year)	Zone	Crop; Variety	Matrix	Total Rate[1] ppm	Total Rate[1] (lb ae/A	PHI (days)	Residues (ppm)[2, 6]	
St, Johns, KS 2007 KS$21	5	Winter Wheat; Jagger	Forage	5.0	2.26[3]	0	0.84	0.89
			Hay		3.39[4]		1.31	1.62
			Grain		6.77		0.32	0.32
			Straw				1.49	1.38
Velva, ND 2007 ND$04	7	Spring Wheat; Glenn	Forage	5.0	2.19[3]	0	0.89	0.94
			Hay		3.29[4]		2.24	2.09
			Grain		6.58		0.30	0.47
			Straw				1.52	0.61

[1] The rate is expressed both in terms of the concentration in the irrigation water (ppm) and the total amount (lb ae/A) applied.
[2] Expressed in acid equivalents. The lower level of method validation (LLMV) is 0.05 ppm.
[3] Harvested after only two applications.
[4] Harvested after only three applications.
[5] The raw data listed residues <LLMV for field corn grain, but only for the grain samples from one test. All other results are noted only as <0.05 ppm, i.e. <LLMV.
[3] The two results for each field trial represent two samples taken from a single plot, not two plots.

TABLE C.4. Summary of Residue Data from Cereal Field Trials with Endothall.

Commodity	Total Applic. Rate[1]	PHI (days)	n	Min.	Max.	HAFT[3]	Median (STMdR)	Mean (STMR)	Std. Dev.
			Residue Levels (ppm)[2]						
Sweet Corn									
K+CWHR	5 ppm (6.75-6.91)	0	2	0.05	0.17	0.17	0.11	0.11	0.085
Forage w/o ears		0	2	0.585	1.23	1.23	0.908	0.908	0.456
Forage w/ears		0	2	0.445	0.97	0.97	0.708	0.708	0.371
Stover w/ears		0	2	0.635	4.88	4.88	2.758	2.758	3.002
Field Corn									
Forage	5 ppm (2.26-3.38)[4]	0	4	0.285	0.385	0.385	0.334	0.334	0.041
Grain	5 ppm (6.75-7.10)	0	4	0.04	0.05	0.05	0.05	0.05	0.005
Stover		0	4	1.44	3.19	3.19	2.08	2.08	0.82
Sorghum									
Forage	5 ppm (2.26-3.38)[4]	0	3	0.35	2.67	2.67	1.262	1.262	1.237
Grain	5 ppm (6.77)	0	3	0.645	1.21	1.21	1.00	1.00	0.311
Stover		0	3	0.96	4.90	4.90	2.91	2.91	1.97
Wheat									
Forage	5 ppm (2.19-3.39)[4]	0	4	0.685	2.13	2.13	1.15	1.15	0.662
Hay		0	4	1.055	3.09	3.09	1.94	1.94	0.89
Grain	5 ppm (6.58-6.77)	0-1	4	0.32	1.91	1.91	0.71	0.71	0.800
Straw		0-1	4	1.07	2.74	2.74	1.83	1.83	0.74
AGF			1	20.3	20.3	20.3	20.3	20.3	N/A

[1] The value in parentheses is the total application rate in terms of lb ae/A.
[2] Residues are expressed in terms of the free acid. The LOQ is 0.05 ppm. For all calculations, the LOQ was used for all values reported ≤LOQ.
[3] HAFT = Highest Average Field Trial.

[4] Field corn forage, sorghum forage, and wheat forage and hay were harvested after only two or three applications.

D. CONCLUSION

The available field trial data are adequate with respect to the following cereal grain commodities: all sweet corn commodities; field corn grain and stover; sorghum grain and stover; and wheat grain and straw. The data support the use of endothall-treated water for irrigation of cereal grains, except rice. The data support the use of endothall in irrigation water at a concentration of 5 ppm ae, with no more that six applications per season, and a minimum 7-day interval between applications to the water. Residues on cereal crops are determined at a 0-day PHI.

However, the residue data on field corn forage, sorghum forage, and wheat forage and hay are not adequate because these commodities did not receive all six possible applications prior to harvest. Separate plots should have been set up using earlier applications of endothall-treated water in order to allow for all six applications to be applied prior the normal harvest of these commodities.

E. REFERENCES

None

F. DOCUMENT TRACKING

RDI: David Soderberg (5 June 2009); William Donovan (5 June 2009)
Petition Number: 8E7419
DP#: 356315
PC Code: 038901 and 038905

Template Version June 2005

Primary Evaluator	David Soderberg, Chemist, HED, RABV	Date: 5 June 2009
Approved by	William Donovan, Senior Scientist, HED, RABV	Date: 5 June 2009

This DER was originally prepared under contract by Dynamac Corporation (1910 Sedwick Road, Building 100, Suite B, Durham, NC 27713; submitted 4/1/2009). The DER has been reviewed by the Health Effects Division (HED) and revised to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORT:

47520713. Arsenovic, M. (2008) Endothall (Hydrothol 191): Magnitude of the Residue on Grain Cereal Group (Except Rice): Lab Project Number: Z9768. Unpublished study prepared by Interregional Research Project No. 4. 590 pages.

EXECUTIVE SUMMARY:

Interregional Research Project No. 4 (IR-4) submitted corn, sorghum and wheat processing studies reflecting the exposure of these crops to endothall through the use of treated irrigation water. For each study, separate field trials were conducted during the 2007 growing season on field corn in IL (Zone 5), grain sorghum in KS (Zone 7), and wheat in TX (Zone 6). For each field trial, a 2.0 lb ae/gal soluble concentrate (SC/L) formulation of endothall (monoamine salt) was used to treat the irrigation water at a rate of 5 ppm ae. [In order to avoid the complications of different molecular weights for different salts, endothall concentrations are expressed as the free acid equivalents (ae).] The treated water was then applied using overhead sprinklers to each crop as six broadcast foliar applications during grain development and maturation at retreatment intervals (RTIs) of 6-8 days. A volume equivalent to 1 acre inch of water (~27,154 gal/A) was applied for each application. Based on the concentration of the endothall in the irrigation water and the amount of water applied, the application rate for endothall was equivalent to 1.12-1.13 lb ae/A/application. The total seasonal application rate was 6.77 lb ae/A for the field corn and sorghum trials and 6.71 lb ae/A for the wheat trial.

Single bulk control and treated samples of mature grain were harvested from each crop at normal maturity, on the day of the last irrigation (0 day after treatment, DAT). The grain samples from each crop were processed using simulated commercial procedures. The corn grain was processed into grits, meal, flour and oil by dry-milling and into starch and oil by wet-milling. The sorghum was processed by dry-milling into flour. The wheat grain was initially cleaned to generate aspirated grain fractions (AGF) and was then milled into germ, bran, middlings, shorts and flour. Samples of each grain, AGF and each processed fraction were stored at ≤-10°C for up to 79 days prior to analysis. The sample storage intervals and conditions are supported by the available storage stability data.

Residues of endothall (free acid) in/on cereal grains, wheat AGF, and each processed fraction were determined using an adequate LC/MS/MS method (Method No. KP-242R1). With the exception of corn oil, residues were extracted with water and then derivatized with heptafluoro-*p*-tolylhydrazine (HFTH) in 50% H_3PO_4. Oil samples were diluted with water and partitioned against hexane, and the remaining aqueous soluble residues were then derivatized with HFTH. The derivatized residues from each matrix were cleaned up by partitioning into methyl t-butyl ether (MTBE) followed by elution through an amine solid phase extraction (SPE) cartridge. Residues were then analyzed by LC/MS/MS using external standards for quantitation.

In the corn grain processing study, endothall residues were <0.05 ppm (<LOQ) in/on the corn grain (RAC) and all its processed fractions. Although processing factors could not be determined for any processed corn fractions, there was no indication of endothall residues concentrating in processed corn commodities.

In the sorghum processing study, endothall residues were 1.49 ppm in/on sorghum grain (RAC) and 1.09 ppm in sorghum flour, indicating that residues were reduced in flour by 0.7x.

In the wheat processing study, endothall residues were 1.34 ppm in/on the bulk sample of grain and 20.3 ppm in/on the composited AGF sample, for a concentration factor of 15x for wheat AGF. Following processing, endothall residues were 3.44 ppm in germ, 3.10 ppm in bran, 1.14 ppm in middlings, 0.75 ppm in flour, and 1.81 ppm in shorts. The resulting processing factors were 2.6x for germ, 2.3x for bran, 0.9x for middlings, 0.6x for flour, and 1.4x for shorts.

<u>STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS</u>:

Under the conditions and parameters used in the study, the corn, wheat and sorghum processing studies are classified as scientifically acceptable. The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document, DP# 356315.

<u>COMPLIANCE</u>:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported which would have an adverse impact on the validity of the study.

A. BACKGROUND INFORMATION

Endothall [7-oxabicyclo[2,2,1] heptane-2,3-dicarboxylic acid] is a selective contact herbicide, defoliant, desiccant, and aquatic algicide that belongs to the dicarboxylic acid chemical class. The free acid of endothall (PC Code 038901) and its dipotassium (PC Code 038904) and amine (PC Code 038905) salts are registered primarily as aquatic herbicides for the control a variety of plants in water bodies, including irrigation canals. They are also registered for desiccation/ defoliation of alfalfa/clover (grown for seed only), cotton, and potatoes prior to harvest, and for reduction of sucker branch growth in hops. Permanent tolerances are established for the combined residues of endothall and its monomethyl ester at 0.1 ppm in/on cotton seeds, fish, dried hops and potatoes, and at 0.05 ppm in/on rice grain and straw [40 CFR §180.293(a)(1)].

In conjunction with a petition for tolerances on a wide variety of irrigated crops (PP# 8E7419), IR-4 has submitted a processing studies for field corn, sorghum and wheat reflecting irrigation of these crops with endothall-treated water. The chemical structure and nomenclature of endothall and its monoamine salt are listed in Table A.1. The physicochemical properties of technical grade endothall and its monoamine salt are listed in Table A.2.

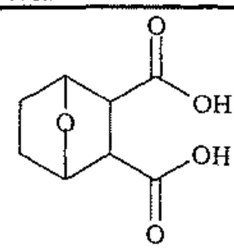
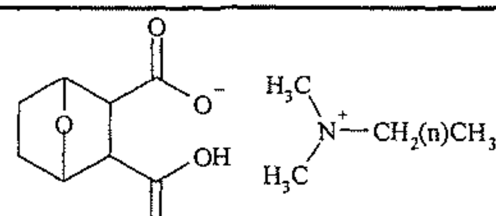
Table A.1. Nomenclature of Endothall and its Monoamine Salt.	
Chemical Structure	
Common name	Endothall
Molecular Formula	$C_8H_{10}O_5$
Molecular Weight	186.16
IUPAC name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid
CAS name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid
CAS #	145-73-3
PC Code	038901
Current Food/Feed Site Registration	Cotton, hops, potato, alfalfa grown for seed
Chemical Structure	 (n = 7-17)
Common name	Endothall, mono-N,N-dimethylalkyl amine salt
Molecular Formula	Not available
Molecular Weight	Average: 422
IUPAC name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid, compound with N,N-dimethylcocoamine
CAS name	Not available
CAS #	66330-88-9
PC Code	038905
Current Food/Feed Site Registration	Cotton, hops, potato, alfalfa grown for seed, aquatic uses

Table A.2. Physicochemical Properties of Endothall and Its Monoamine Salt.

Parameter	Value	Reference
Endothall (acid)		
Melting point	108-110℃	D187593, D187590, and D187588, 5/5/93, K. Dockter
pH	2.7 at 25℃ (1% solution)	D187593, D187590, and D187588, 5/5/93, K. Dockter
Density, bulk density, or specific gravity	0.481 g/cm^3 (bulk) at 25℃	D187593, D187590, and D187588, 5/5/93, K. Dockter
Water solubility at 25℃	109.8 g/L 13.1 g/100 mL in water, pH 5 12.7 g/100 mL in water, pH 7 12.5 g/100 mL in water, pH 9	D166798, 7/2/92, K. Dockter D207011, 9/30/94, F. Toghrol
Solvent solubility at 25℃	3.4 g/100 mL in acetonitrile 2.4 g/100 mL in n-octanol 16.0 g/100 mL in tetrahydrofuran	D207011, 9/30/94, F. Toghrol
Vapor pressure	3.92 x 10^{-5} mm Hg at 24.3℃	D166798, 7/2/92, K. Dockter
Dissociation constant, pK_a	4.32 for Step 1 and 6.22 for Step 2 at 20℃ (0.2% solution in 20% basic ethanol); dissociation rate 1.8-2.3 x 10^3 μmho within 3-5 minutes at □25℃, by conductivity meter	D188708, 5/3/93, K. Dockter
Octanol/water partition coefficient	Not applicable to endothall acid	D166798, 7/2/92, K. Dockter
UV/visible absorption spectrum	Not available	
Endothall, mono-N,N-dimethylalkyl amine salt		
Boiling point	Not available	
pH	5.2 at 25℃ (1% solution)	D187593, D187590, and D187588, 5/5/93, K. Dockter
Density, bulk density, or specific gravity	1.028 g/mL at 25℃	D187593, D187590, and D187588, 5/5/93, K. Dockter
Water solubility at 25℃	≥49.2 g/100mL in water, pH 5 ≥51.6 g/100 mL in water, pH 7 ≥49.8 g/100 mL in water, pH 9	D210814, 8/9/95, S. Knizner
Solvent solubility at 25℃	≥102.5 g/100mL in acetonitrile ≥95.4 g/100 mL in n-octanol ≥104.3 g/100 mL in tetrahydrofuran	D210814, 8/9/95, S. Knizner
Vapor pressure	2.09 x 10^{-5} mm Hg at 25℃ (calculated; mixed mono- and dialkylamine (C8-C20))	D206344, 9/22/94, F. Toghrol
Dissociation constant, pK_a	4.24 for Step 1 and 6.07 for Step 2 at 20℃ for mixed mono- and dialkylamine (C8-C20) in acidified ethanol/water; dissociation complete □17 minutes (1.7 x 10^3 μmho) at 25℃	D198885, 4/7/94, F. Toghrol
Octanol/water partition coefficient	K_{OW} 2.097 at concentrations of 8.9 x 10^{-7} M and 8.9 x 10^{-4} M, at 25℃	D209995, 1/20/95, L. Edwards
UV/visible absorption spectrum	Not available	

B. EXPERIMENTAL DESIGN

B.1. Application and Crop Information

In three field trials conducted in IL, KS and TX during 2007, separate fields of field corn, sorghum and wheat were irrigated with endothall-treated water using overhead sprinklers (Table B.1.I). The irrigation water was treated with endothall (2.0 lb ae/gal SC/L monoamine salt) at a concentration of ~5 ppm, acid equivalent. Each cereal grain crop was irrigated six times during seed head formation and development at RTIs of 6-8 days. A volume equivalent to ~1 acre inch of water (27,154 gal/A) was applied for each irrigation. Based on the concentration of the endothall in the irrigation water and the amount of water applied, application rate for endothall was equivalent to 1.12-1.13 lb ae/A/application, for a total of 6.7-6.77 lb ae/A/season (1x target rate).

TABLE B.1.1. Study Use Pattern.

Location (City, State; Year) Trial ID	End-Use Product	Application Information					
		Method [1]; Timing	Concen. [2]	Volume (gal/A) [3]	Single Rate (lb ae/A) [4]	RTI [5] (days)	Total Rate (lb ae/A) [4]
Corn Field Trial							
Sparta, IL 2007 IL$09	2.0 lb ae/gal SC/L	Six broadcast foliar applications from 13-14 true leaves	5.0	27,154	1.13	6-8	6.77
Sorghum Field Trial							
Larned, KS 2007 KS$03	2.0 lb ae/gal SC/L	Six broadcast foliar applications from early dough (BBCH 83) to maturity (BBCH 89)	5.0	27,161	1.13	6-7	6.77
Wheat Field Trial							
Bernard, TX 2007 TX$19	2.0 lb ae/gal SC/L	Six broadcast foliar applications from end of flowering (BBCH 69) to maturity (BBCH 89)	5.0	26,926-26,938	1.12	6-8	6.71

1 All applications were made using overhead sprinkler systems.
2 The concentration of endothall (in acid equivalents) in the irrigation water. No adjuvants were included in the irrigation water.
3 The target irrigation rate was 1 acre inch of water or 27,154 gal/A.
4 The equivalent field use rates were calculated by the reviewer based on the concentration of the endothall (ae), the application volume and plot size.
5 RTI = Retreatment Interval.

B.2. Sample Handling and Processing Procedures

Single control and treated bulk samples of corn grain (~300 lb/sample), sorghum grain (~50 lb/sample), and wheat grain (472-615 lb/sample) were harvested at 0 DAT. The grain samples were stored frozen at the field sites and shipped 7-21 days later by ACDS Freezer truck to the processing facility, GLP Technologies (Navasota, TX), where the samples were stored at ≤-12°C until processing. Processing of each grain sample was completed within 23-52 days of harvest.

For corn grain, the bulk samples were dried and cleaned by aspiration and screening, but no AGF sample was collected. The cleaned corn grain was dry-milled in grits, meal, flour, bran and germ, and the germ was then extracted for oil (Figure B.1). A separate subsample of corn grain was also wet-milled into starch and germ, with the germ being extracted for oil.

The bulk samples of sorghum grain were dried and cleaned by aspiration and screening, but no AGF sample was collected. The cleaned grain was then processed into flour by dry-milling (Figure B.2)

The bulk sample of wheat grain also cleaned by aspiration and screening, and the resulting AGF was separated into the following particle size classes: <425 μm, >425 μm, 850 μm, 1180 μm,

>2000 µm, and >2360 µm (Figure B.3). The fractions <2360 µm were recombined to form the AGF sample. The cleaned wheat grain was then milled into the following fractions: germ, middlings, bran, flour and shorts (Figure B.4).

Following processing, the samples of grain, AGF and each processed fraction were transferred to frozen storage (≤-12°C). The frozen samples were shipped, 2-7 days after processing, by overnight courier on dry ice to the analytical laboratory, United Phosphorus, Inc. (King or Prussia, PA), where the samples were stored at ≤-18°C until analysis.

FIGURE B.1. Processing Flowchart for Field Corn

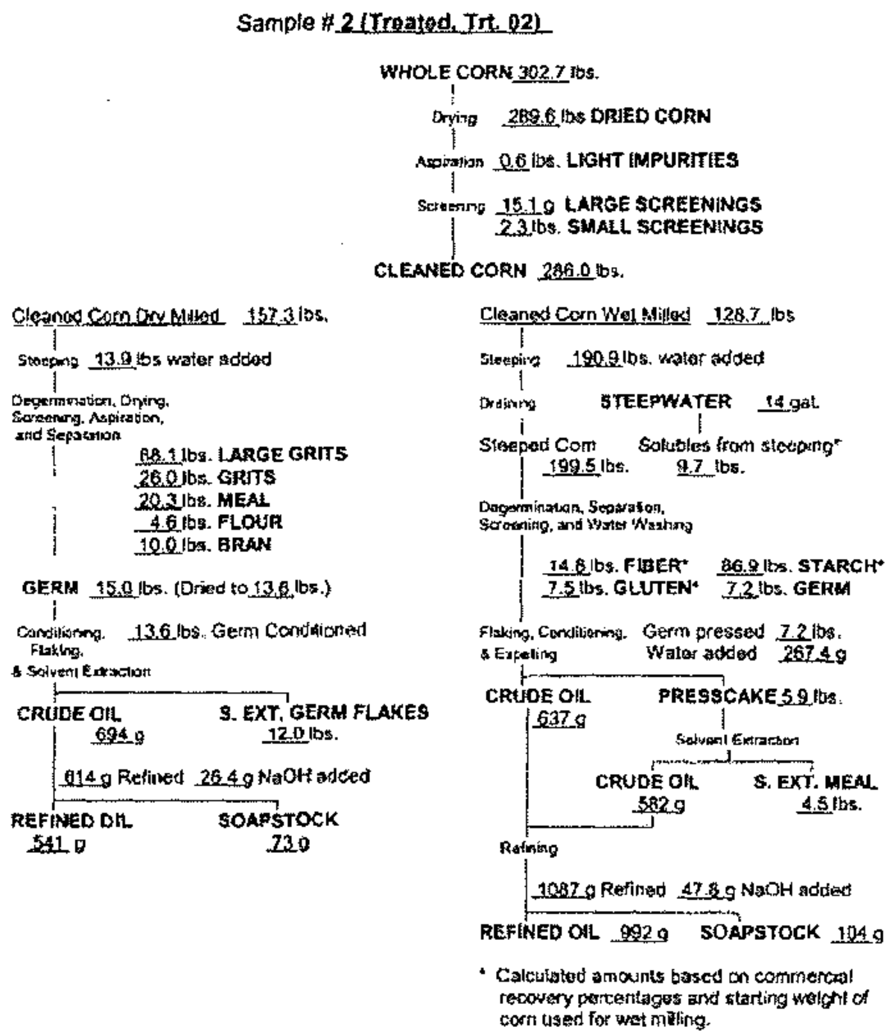


FIGURE B.2. Processing flowchart for Grain Sorghum

Sample # 2 (Treated, Trt. 02)

GRAIN SORGHUM 43.3 lbs.

Drying — 39.6 lbs. after drying

Aspiration — 3.5 lbs. LIGHT IMPURITIES

Screening — 10.3 g. LARGE SCREENINGS
3.8 lbs. SMALL SCREENINGS
32.2 lbs. CLEANED SEED

Decortication 9.0 lbs. used

BRAN 0.7 lbs | BREAK FLOUR 1.2 lbs | REDUCTION FLOUR 1.2 lbs

2.3 lbs COMBINED FLOUR

5.9 lbs. Waste material

FIGURE B.3. Processing flowchart for Wheat Aspirated Grain Fractions.

COMMODITY 477.7 lbs.

Drying n/a lbs. (no drying)

477.7 lbs. used for generation

Aspiration 0.2 lbs.

Classification

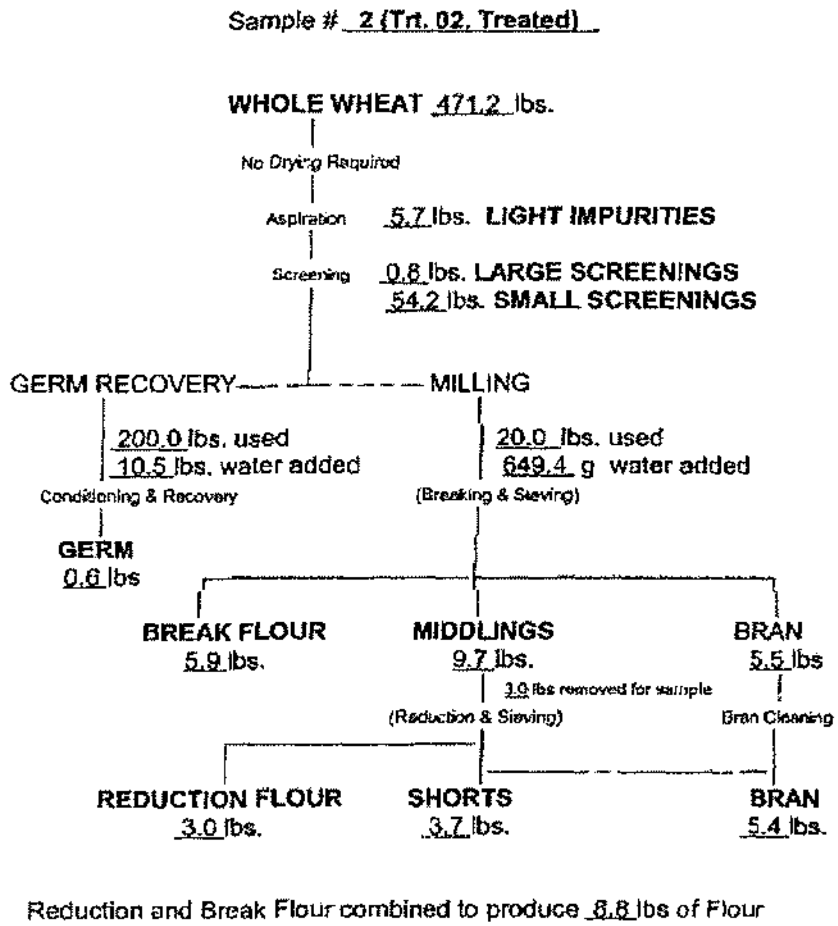
- ASPIRATED GRAIN FRACTION > 2360 micron 16.9 g
- ASPIRATED GRAIN FRACTION > 2000 micron 2.0 g
- ASPIRATED GRAIN FRACTION > 1180 micron 1.8 g
- ASPIRATED GRAIN FRACTION > 850 micron 0.7 g
- ASPIRATED GRAIN FRACTION > 425 micron 7.6 g
- ASPIRATED GRAIN FRACTION < 425 micron 38.8 g

RECOMBINATION

2.0 g < 2360 micron and > 2000 micron
1.8 g > 1180 micron
0.7 g > 850 micron
7.5 g > 425 micron
38.7g < 425 micron

ASH CONTENT: 8.2 %

FIGURE B.4. Processing Flowchart for Wheat Grain.



B.3. Analytical Methodology

Residues of endothall (free acid) in/on cereal grain and cereal grain processed fractions were determined using a LC/MS/MS method (Method No. KP-242R1) entitled “Analytical Method for Determination of Endothall in Crops”, issued 5/4/2007.

With the exception of corn oil, residues were extracted twice by homogenization with water followed by centrifugation and filtering. For corn oil, the sample was mixed with water and partitioned three times against hexane, discarding the hexane phases. The aqueous soluble residues from each fraction were then derivatized with HFTH in 50% H_3PO_4 at 100-120°C for 90 minutes. After cooling, the derivatized residues were then partitioned into MTBE, evaporated to dryness, and reconstituted in hexane:MTBE (1:1 v/v). Residues were next cleaned using an amine SPE cartridge eluted with methanol:MTBE (4:1,v/v). Residues were analyzed by LC/MS/MS using external standards. The m/z 397→166 ion transition was used for quantifying residues. Residues are expressed in endothall acid equivalents. The validated LOQ for endothall in/on each commodity is 0.05 ppm. An LOD of 0.00001 ppm was reported; however, this value was the instrument LOD, rather than the LOD of residues in a control matrix.

For method validation, control samples of corn grain and flour and wheat grain and bran were each fortified with endothall at 0.05-5.0 ppm and control samples of wheat AGF were fortified with endothall at 0.05-20 ppm. For concurrent recoveries, control samples of the various commodities were fortified with endothall at 0.05-4.0 ppm.

C. RESULTS AND DISCUSSION

The LC/MS/MS method used for determining residues of endothall in/on cereal grains, processed fractions, and wheat AGF was adequately validated prior to and in conjunction with the analysis of processing study samples. Average method validation recoveries (±SD) were 88 ± 6% for corn grain, 78 ± 9% for corn flour, 78 ± 3% for wheat grain, 79 ± 6% for wheat bran, and 80 ± 9% for wheat AGF (Table C.1). Average concurrent recoveries were 73-87% from corn commodities, 75-78% from sorghum commodities, and 74-78% from wheat commodities. Apparent residues of endothall were <LOQ in/on control samples of each matrix, with the exception of wheat AGF. The control sample of wheat AGF had apparent endothall residues at 0.105 ppm. Adequate sample calculations and example chromatograms were provided, and the fortification levels used for the method recoveries were similar in magnitude to the measured residue levels.

Samples were stored at <-18°C for up to 79 days prior to analysis (Table C.2). Adequate storage stability data are available indicating that endothall is stable for up to 465-469 days in frozen tomatoes, lettuce, corn grain and sugar beet roots and up to 316 days in frozen soybeans (47520719.der, under review). These stability data will support the storage durations and conditions for the cereal grain processing studies.

Following six overhead sprinkler applications of endothall (monoamine salt) to field corn at rates totaling 6.77 lb ae/A, residues in whole grain (RAC) were <0.05 ppm at 0 DAT, and the residues were also <0.05 ppm in all the resulting processed fractions (Table C.3). Although processing factors could not be determined for any processed corn fractions, there was no indication of endothall residues concentrating in processed corn commodities.

Following six overhead sprinkler applications of endothall (monoamine salt) to grain sorghum at rates totaling 6.77 lb ae/A, residues were 1.49 in/on whole grain (RAC) harvested at 0 DAT. Residues were 1.09 ppm in flour, indicating that residues were reduced by 0.7x in sorghum flour.

Following six overhead sprinkler applications of endothall (monoamine salt) to wheat at rates totaling 6.71 lb ae/A, residues were 1.34 in/on the bulk sample of wheat grain (RAC) harvested at 0 DAT. After cleaning and aspiration of the grain, residues in the composited sample of AFG were 20.3 ppm. Residues concentrated by 15x in the AGF sample indicating that endothall residues occur primarily as surface residues on wheat grain. Following processing, endothall residues were 3.44 ppm in wheat germ, 3.10 ppm in bran, 1.14 ppm in middlings, 0.75 ppm in flour, and 1.81 ppm in shorts. The resulting processing factors were 2.6x for germ, 2.3x for bran, 0.9x for middlings, 0.6x for flour, and 1.4x for shorts. The higher concentration of residues in wheat bran and germ are further evidence that endothall residues were primarily associated with the outer surface of the grain.

TABLE C.1. Summary of Method Validation and Concurrent Recoveries of Endothall from Cereal Grains.

Crop	Matrix	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean ± Std. Dev. (%)
Method Validation					
Corn	Grain	0.05	3	96, 81, 93	90 ± 8
		0.5	3	80, 92, 90	87 ± 6
		5.0	3	88, 86, 83	86 ± 3
		Total	**9**	**80-96**	**88 ± 6**
	Flour	0.05	3	72, 71, 77	73 ± 3
		0.5	3	85, 74, 74	78 ± 6
		5.0	3	79, 73, 99	84 ± 14
		Total	**9**	**71-99**	**78 ± 9**
Wheat	Grain	0.05	3	75, 76, 73	75 ± 2
		0.5	3	76, 72, 72	73 ± 2
		5.0	3	83, 73, 77	78 ± 5
		Total	**9**	**72-83**	**75 ± 3**
	AGF	0.05	2	79, 100	90
		0.5	2	80, 81	81
		5.0	2	74, 73	74
		20	3	75, 73, 88	79 ± 8
		Total	**9**	**73-100**	**80 ± 9**
	Bran	0.05	3	84, 91, 83	86 ± 4
		0.5	3	78, 79, 71	76 ± 4
		5.0	3	74, 77, 76	76 ± 2
		Total	**9**	**71-91**	**79 ± 6**
Concurrent Recoveries					
Corn	Grain	0.05	1	72	77
		0.2	1	81	
	Oil	0.05	1	71	73
		0.5	1	74	
	Grits	0.05	1	73	87
		1.0	1	101	
	Meal	0.05	1	72	74
		0.5	1	76	
Sorghum	Grain	0.05	1	77	75
		1.0	1	72	
	Flour	0.05	1	79	78
		1.0	1	76	

TABLE C.1. Summary of Method Validation and Concurrent Recoveries of Endothall from Cereal Grains.

Crop	Matrix	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean ± Std. Dev. (%)
Wheat	Grain	0.05	4	71	74
		1.0	1	77	
	Middlings	0.05	1	79	78
		2.0	1	77	
	Flour	0.05	1	73	74
		0.5	1	74	
	Germ	0.05	1	73	74
		3.0	1	75	
	Shorts	0.05	1	77	75
		4.0	1	73	

1 Standard deviations are calculated for data sets having ≥3 values.

TABLE C.2. Summary of Storage Conditions.

Matrix	Storage Temperature (°C)	Actual Storage Duration (days)[1]	Interval of Demonstrated Storage Stability (days)[2]
Sorghum grain and flour	≤-10	26	306-466
Wheat grain		79	
Wheat middlings, bran, flour, shouts and germ		34-45	
Corn grain, grits, meal, flour, starch, and oil		22-37	

1 Interval from harvest to extraction for analysis. Extracts were stored up to 10 days prior to analysis.
2 Endothall is stable under frozen conditions for up to 465 days in corn grain and 305 days in soybean seed and oil (47520719.der, under review).

TABLE C.3. Residue Data from Grain Processing Studies with Endothall Monoamine Salt (SC/L).

Crop	Commodity	Total Rate [1]		PHI (days)	Residues [2] (ppm)	Processing Factor
		ppm	lb ae/A			
Field Corn	Grain (RAC)	5.0	6.77	0	<0.05	--
	Grits				<0.05	NC
	Meal				<0.05	NC
	Flour				<0.05	NC
	Starch				<0.05	NC
	Oil, refined (wet milled)				<0.05	NC
	Oil, refined (dry milled)				<0.05	NC
Sorghum	Grain (RAC)	5.0	6.77	0	1.49	--
	Flour				1.09	0.7x

TABLE C.3. Residue Data from Grain Processing Studies with Endothall Monoamine Salt (SC/L).

Crop	Commodity	Total Rate [1]		PHI (days)	Residues [2] (ppm)	Processing Factor
		ppm	lb ae/A			
Wheat	Grain (RAC)	5.0	6.71	0	1.34	--
	AGF				20.3 [4]	15x
	Bran				3.10	2.3x
	Middlings				1.14	0.9x
	Flour				0.747	0.6x
	Shorts				1.81	1.4x
	Germ				3.44	2.6x

[1] The rate is expressed both in terms of the concentration in the irrigation water (ppm) and the total amount (lb ae/A) applied.
[2] Expressed in acid equivalents. The LOQ is 0.05 ppm for each commodity.
[3] Average of two samples (2.01 and 1.80 ppm).
[4] Average of three analyses on a single sample.
NC = not calculated, as residues were <LOQ in the RAC and all processed fractions

D. CONCLUSION

The cereal grain processing studies are adequate. Although residues were <LOQ in/on corn grain, endothall residues did not appear to concentrate in any corn grain processed fractions. For sorghum, endothall residues were reduced in flour (0.7x). For wheat, endothall residues were shown to concentrate substantially in AGF (15x) and to lesser extent in bran, germ and shorts (1.4x-2.6x). Residues were reduced in both wheat middlings and flour (0.6x-0.9x).

E. REFERENCES

None

F. DOCUMENT TRACKING

RDI: David Soderberg (5 June 2009); William Donovan (5 June 2009)
Petition Number: 8E7419
DP#: 356315
PC Code: 038901 and 038905

Template Version June 2005

Primary Evaluator	David Soderberg, Chemist, RABV, HED	Date: 5 June 2009
Approved by	William Donovan, Senior Scientist, RABV, HED	Date: 5 June 2009

This DER was originally prepared under contract by Dynamac Corporation (1910 Sedwick Road, Building 100, Suite B, Durham, NC 27713; submitted 3/31/2009). The DER has been reviewed by the Health Effects Division (HED) and revised as needed for clarity, correctness and to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORT:

47520715. Arsenovic, M. (2008) Endothall (Hydrothol 191): Magnitude of the Residue on Animal Feed Nongrass Group: Lab Project Number: Z9756. Unpublished study prepared by Interregional Research Project No. 4. 226 pages.

EXECUTIVE SUMMARY:

Interregional Research Project No. 4 (IR-4) submitted field trial data reflecting the exposure of alfalfa to endothall through the use of treated irrigation water. In two alfalfa field trials conducted during 2007 in Zones 5 and 7, a 2.0 lb ae/gal soluble concentrate (SC/L) formulation of endothall (monoalkylamine salt) was used to treat the irrigation water at a rate of 5 ppm ae. [In order to avoid the complications of different molecular weights for different salts, endothall concentrations are expressed as the free acid equivalents (ae).] The treated water was applied to the alfalfa during vegetative development as six broadcast foliar applications using overhead sprinklers, at retreatment intervals (RTIs) of 6-8 days. A volume equivalent to ~1 acre inch of water (27,000 gal/A) was applied for each application. Based on the concentration of the endothall in the irrigation water and the amount of water applied, the application rates for endothall were equivalent to 0.99-1.10 lb ae/A/application, for a total of 5.94-6.58 lb ae/A/season.

Duplicate control and treated samples of alfalfa forage and hay were harvested from each test on the day of the final application (0 days after treatment, DAT), and the hay samples were field-dried for 1-5 days prior to collection. After collection, samples were stored at ≤-18°C for up to 83 days prior to analysis. Adequate storage stability data are available to support the duration and conditions of sample storage.

Residues of endothall (free acid) in/on alfalfa forage and hay were determined using an adequate LC/MS/MS method (Method No. KP-242R1). For this method, residues were extracted with water and then derivatized with heptafluoro-*p*-tolylhydrazine (HFTH) in 50% H_3PO_4. The derivatized residues were cleaned up by partitioning into methyl t-butyl ether (MTBE) and elution through an amine solid phase extraction (SPE) cartridge. Residues were then analyzed by LC/MS/MS using external standards for quantitation. Residues are expressed in endothall

acid equivalents. The validated limit of quantitation (LOQ) for endothall in/on forage and hay is 0.05 ppm.

Following six overhead sprinkler applications with irrigation water containing endothall at 5 ppm (5.94-6.58 lb ae/A/season), endothall residues were 1.41-2.24 ppm in/on four forage samples and 3.09-5.31 ppm in/on four hay samples harvested at 0 DAT. Average endothall residues were 1.95 ppm for forage and 4.57 ppm for hay, and the highest average field trial (HAFT) residues were 2.12 ppm for forage and 4.93 ppm for hay. No residue decline data were provided.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the alfalfa field trial residue data are classified as scientifically acceptable. Although limited field trials were performed, these applications are expected to be conservative relative to actual inadvertent applications. The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document, DP# 356315.

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported which would have an adverse impact on the validity of the study.

A. BACKGROUND INFORMATION

Endothall [7-oxabicyclo[2,2,1] heptane-2,3-dicarboxylic acid] is a selective contact herbicide, defoliant, desiccant, and aquatic algicide that belongs to the dicarboxylic acid chemical class. The free acid of endothall (PC Code 038901) and its dipotassium (PC Code 038904) and alkylamine (PC Code 038905) salts are registered primarily as aquatic herbicides for the control a variety of plants in water bodies. , including irrigation canals. They are also registered for desiccation/ defoliation of alfalfa/clover (grown for seed only), cotton, and potatoes prior to harvest, and for reduction of sucker branch growth in hops. Permanent tolerances are established for the combined residues of endothall and its monomethyl ester at 0.1 ppm in/on cotton seeds, fish, dried hops and potatoes, and at 0.05 ppm in/on rice grain and straw [40 CFR §180.293(a)(1)].

In conjunction with a petition for tolerances on a wide variety of irrigated crops (PP# 8E7419), IR-4 has submitted field trial data reflecting irrigation of alfalfa with endothall-treated water. The chemical structure and nomenclature of endothall and its monoalkylamine salt are listed in Table A.1. The physicochemical properties of technical grade endothall and its monoalkylamine salt are listed in Table A.2.

Table A.1. Nomenclature of Endothall and its Monoalkylamine Salt.

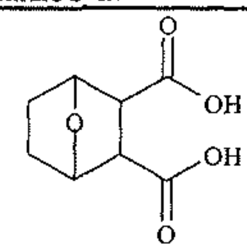
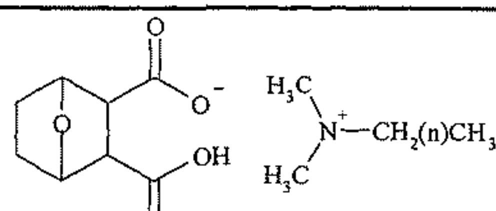
Chemical Structure	
Common name	Endothall
Molecular Formula	$C_8H_{10}O_5$
Molecular Weight	186.16
IUPAC name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid
CAS name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid
CAS #	145-73-3
PC Code	038901
Current Food/Feed Site Registration	Cotton, hops, potato, alfalfa grown for seed
Chemical Structure	 (n = 7-17)
Common name	Endothall, mono-N,N-dimethylalkyl amine salt
Molecular Formula	Not available
Molecular Weight	Average: 422
IUPAC name	7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid, compound with N,N-dimethylcocoamine
CAS name	Not available
CAS #	66330-88-9
PC Code	038905
Current Food/Feed Site Registration	Cotton, hops, potato, alfalfa grown for seed, aquatic uses

Table A.2. Physicochemical Properties of Endothall and Its Monoalkylamine Salt.

Parameter	Value	Reference
Endothall (acid)		
Melting point	108-110°C	D187593, D187590, and D187588, 5/5/93, K. Dockter
pH	2.7 at 25°C (1% solution)	D187593, D187590, and D187588, 5/5/93, K. Dockter
Density, bulk density, or specific gravity	0.481 g/cm^3 (bulk) at 25°C	D187593, D187590, and D187588, 5/5/93, K. Dockter
Water solubility at 25°C	109.8 g/L 13.1 g/100 mL in water, pH 5 12.7 g/100 mL in water, pH 7 12.5 g/100 mL in water, pH 9	D166798, 7/2/92, K. Dockter D207011, 9/30/94, F. Toghrol
Solvent solubility at 25°C	3.4 g/100 mL in acetonitrile 2.4 g/100 mL in n-octanol 16.0 g/100 mL in tetrahydrofuran	D207011, 9/30/94, F. Toghrol
Vapor pressure	3.92 x 10^{-5} mm Hg at 24.3°C	D166798, 7/2/92, K. Dockter
Dissociation constant, pK$_a$	4.32 for Step 1 and 6.22 for Step 2 at 20°C (0.2% solution in 20% basic ethanol); dissociation rate 1.8-2.3 x 10^3 µmho within 3-5 minutes at □25°C, by conductivity meter	D188708, 5/3/93, K. Dockter
Octanol/water partition coefficient	Not applicable to endothall acid	D166798, 7/2/92, K. Dockter
UV/visible absorption spectrum	Not available	
Endothall, mono-N,N-dimethylalkyl amine salt		
Boiling point	Not available	
pH	5.2 at 25°C (1% solution)	D187593, D187590, and D187588, 5/5/93, K. Dockter
Density, bulk density, or specific gravity	1.028 g/mL at 25°C	D187593, D187590, and D187588, 5/5/93, K. Dockter
Water solubility at 25°C	≥49.2 g/100mL in water, pH 5 ≥51.6 g/100 mL in water, pH 7 ≥49.8 g/100 mL in water, pH 9	D210814, 8/9/95, S. Knizner
Solvent solubility at 25°C	≥102.5 g/100mL in acetonitrile ≥95.4 g/100 mL in n-octanol ≥104.3 g/100 mL in tetrahydrofuran	D210814, 8/9/95, S. Knizner
Vapor pressure	2.09 x 10^{-5} mm Hg at 25°C (calculated; mixed mono- and dialkylamine (C8-C20))	D206344, 9/22/94, F. Toghrol
Dissociation constant, pK$_a$	4.24 for Step 1 and 6.07 for Step 2 at 20°C for mixed mono- and dialkylamine (C8-C20) in acidified ethanol/water; dissociation complete □17 minutes (1.7 x 10^3 µmho) at 25°C	D198885, 4/7/94, F. Toghrol
Octanol/water partition coefficient	K_{OW} 2.097 at concentrations of 8.9 x 10^{-3} M and 8.9 x 10^{-4} M, at 25°C	D209995, 1/20/95, L. Edwards
UV/visible absorption spectrum	Not available	

B. EXPERIMENTAL DESIGN

B.1. Study Site Information

Two alfalfa field trials were conducted in Zones 5 and 7 during 2007 (Table B.1.1). The irrigation water used in each test was treated with endothall (2.0 lb ae/gal SC monoalkylamine salt) at a concentration of ~5 ppm, acid equivalent. The treated water was applied to the alfalfa during vegetative development as six broadcast foliar applications using overhead sprinklers, at

RTIs of 6-8 days. A volume equivalent to ~1 acre inch of water (~27,154 gal/A) was applied for each application. Based on the concentration of the endothall and the amount of water applied, application rates for endothall were equivalent to 0.99-1.10 lb ae/A/application, for a total of 5.94-6.58 lb ae/A/season (Table B.1.3). These applications are expected to be conservative relative to actual applications.

TABLE B.1.1. Trial Site Conditions.

Trial Identification (City, State; Year)	Soil characteristics[1]			
	Type	%OM	pH	CEC (meq/100g)
Velva, ND 2007 ND$20	Loam	3.2	5.6	17.8
Tilden, IL 2007 IL$30	Silt	2.8	5.6	10.8

[1]These parameters are optional except in cases where their value affects the use pattern for the chemical.

TABLE B.1.2. Water Characterization.

Study site	Water characteristics				
	Type	Hardness/Salinity	pH	Turbidity	Dissolved OM
Velva, ND 2007 ND$20	Well	NR	NR	NR	NR
Tilden, IL 2007 IL$30	City water	NR	NR	NR	NR

NR = not reported.

The actual temperature recordings and rainfall were typical for each site and no unusual weather conditions were reported. No irrigation was reported during the study period. The tests were conducted according to normal agricultural practices for the regions, and information was provided on maintenance pesticides and fertilizers used at each site. No information was provided on the characteristics of the water used for irrigation, other than the source (Table B.1.2).

TABLE B.1.3. Study Use Pattern.

Location (City, State; Year) Trial ID	End-Use Product	Application Information					
		Method; Timing	Concen. [1]	Volume (gal/A) [2]	Single Rate (lb ae/A) [3]	RTI [4] (days)	Total Rate (lb ae/A) [3]
Velva, ND 2007 ND$20	2.0 lb ae/gal SC/L	Six broadcast foliar application during vegetative development using overhead sprinklers.	5.0	26,365	1.10	7	6.58
Tilden, IL 2007 IL$30	2.0 lb ae/gal SC/L	Six broadcast foliar application during vegetative development using overhead sprinklers.	5.0	21,679	0.99	6-8	5.94

[1] The concentration of endothall (in acid equivalents) in the irrigation water. No adjuvants were included in the irrigation water.
[2] The target irrigation rate was 1 acre inch of water or 27,154 gal/A.
[3] The equivalent field use rates were calculated by the reviewer based on the concentration of the endothall (ae), the application volume and plot size.
[4] RTI = Retreatment Interval.

TABLE B.1.4. Trial Numbers and Geographical Locations.

NAFTA Growing Zones[3]	Alfalfa		
	Submitted	Requested[1]	
		Canada	U.S.
1	--	--	1
2	--	--	1
3	--	--	--
4	--	--	--
5	1	--	6
6	--	--	--
7	1	--	1
8	--	--	--
9	--	--	1
10	--	--	1
11	--	--	1
12	--	--	--
13	--	--	--
Total	2	--	12 [9][2]

[1] Based on EPA OPPTS Guideline 860.1500.
[2] The number in brackets indicates a 25% reduction required to support a crop group tolerance.
[3] Regions 1A, 5A and B, 7A and 14-21 are not included in this table as the proposed use is for the U.S. only.

B.2. Sample Handling and Preparation

Alfalfa forage and hay samples were cut at 0 DAT (after the sixth application). Duplicate treated and control samples of forage (≥2.0 lbs) were collected immediately after harvest and placed into frozen storage within 1 hour. The hay was allowed to field-dried for 1-5 days prior to sampling. Duplicate control and treated samples of hay were then place in frozen storage within 1 hour of collection. Samples were stored frozen at the field sites for 10-16 days. Samples were then shipped by ACDS freezer truck to the analytical laboratory, Cerexagri, Inc. (King of Prussia, PA), and stored frozen (≤-18EC) prior to analysis.

B.3. Analytical Methodology

Residues of endothall (free acid) in/on alfalfa forage and hay were determined using a LC/MS/MS method (Method No. KP-242R1) entitled "Analytical Method for Determination of Endothall in Crops", issued 5/4/2007.

For this method, residues were extracted twice by homogenization with water followed by centrifugation and filtering. Residues were then derivatized with HFTH in 50% H_3PO_4 at 100-120°C for 90 minutes. After cooling, the derivatized residues were partitioned into MTBE, evaporated to dryness, and reconstituted in hexane:MTBE (1:1 v/v). Residues were then cleaned using an amine SPE cartridge eluted with methanol:MTBE (4:1,v/v). Residues were analyzed by LC/MS/MS using external standards. The m/z 397→166 ion transition was used for quantifying residues. Residues are expressed in endothall acid equivalents. The validated LOQ for endothall in/on forage and hay is 0.05 ppm. An LOD of 0.00001 ppm was reported; however, this value was the instrument LOD, rather than the LOD of residues in a control matrix.

Control samples of forage and hay were fortified with endothall at 0.05-5.0 ppm for method validation and at 0.05-2.0 ppm for the concurrent recoveries.

C. RESULTS AND DISCUSSION

The LC/MS/MS method used for determining residues of endothall in/on alfalfa was adequately validated prior to and in conjunction with the analysis of field trial samples. Average method validation recoveries (± SD) were 82 ± 7% for forage and 81 ± 9% for hay (Table C.1). Average concurrent recoveries (±SD) were 79 ± 9% for forage and 79 ± 4% for hay. Apparent residues of endothall were <LOQ in/on all control samples. Adequate sample calculations and example chromatograms were provided, and the fortification levels used for the method recoveries were similar in magnitude to the measured residue levels.

Forage and hay samples were stored at ≤-18°C for up to 66 and 83 days, respectively, prior to analysis (Table C.2). Adequate storage stability data are available indicating that endothall is stable in frozen lettuce, corn grain and sugar beet roots for up to 465 days (47520719.der, under review). These stability data will support the storage durations and conditions for the current alfalfa field trials.

Following six overhead sprinkler applications with irrigation water containing endothall at 5 ppm (5.94-6.58 lb ae/A/season), endothall residues were 1.41-2.24 ppm in/on four forage samples and 3.09-5.31 ppm in/on four hay samples harvested at 0 DAT (Table C.3). Average endothall residues were 1.94 ppm for forage and 4.56 ppm for hay, and the HAFT residues were 2.12 ppm for forage and 4.93 ppm for hay (Table C.4). No residue decline data were provided.

No phytotoxicity on the treated alfalfa was reported at either test site. Common cultural practices were used to maintain plants, and the weather conditions and maintenance chemicals and fertilizer used in this study did not have a notable impact on the residue data.

TABLE C.1. Summary of Method Validation and Concurrent Recoveries of Endothall from Alfalfa.

Matrix	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean ± Std. Dev. (%)
Method Validation				
Forage	0.05	3	71, 80, 80	77 ± 5
	0.5	3	96, 83, 83	87± 8
	5.0	3	85, 81, 76	81 ± 5
	Total	9	71-96	82 ± 7
Hay	0.05	3	74, 96, 87	86 ± 11
	0.5	3	94, 78, 75	82 ± 10
	5.0	3	79, 77, 71	76 ± 4
	Total	9	71-96	81 ± 9

TABLE C.1. Summary of Method Validation and Concurrent Recoveries of Endothall from Alfalfa.

Matrix	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean ± Std. Dev. (%)
Concurrent Recoveries				
Forage	0.05	2	70, 74	72
	1.0	1	80	80
	2.0	1	91	91
	Total	4	70-91	79 ± 9
Hay	0.05	2	85,76	81
	1.0	1	78	78
	2.0	1	77	77
	Total	4	76-85	79 ± 4

1 Standard deviations are calculated for data sets having ≥3 values.

TABLE C.2. Summary of Storage Conditions.

Matrix	Storage Temperature (°C)	Actual Storage Duration (days)[1]	Interval of Demonstrated Storage Stability (days)[2]
Forage	≤-18	66	469
Hay		73-83	

1 Interval from harvest to extraction for analysis. Extracts were stored 1-7 days prior to analysis.
2 Based on storage stability data from frozen tomatoes, lettuce, corn grain, sugar beet roots, and soybean seeds (47520719.der, under review).

TABLE C.3. Residue Data from Alfalfa Crop Field Trials with Endothall Monoalkylamine Salt (SC/L).

Trial ID (City, State; Year)	Zone	Crop; Variety	Matrix	Total Rate[1]		PHI (days)[2]	Residues (ppm)[3,4]	
				ppm	lb ae/A			
Velva, ND 2007 ND$20	7	Alfalfa; NK919	Forage		6.58	0	2.13	1.41
			Hay				4.98	4.87
Tilden, IL 2007 IL$30	5	Alfalfa; cattleman's	Forage		5.94	0	2.24	1.99
			Hay				5.31	3.09

1 The rate is expressed both in terms of the concentration in the irrigation water (ppm) and the total amount (lb ae/A) applied.
2 The hay samples were cut at 0 DAT and field-dried for 1 or 5 days prior to collection.
3 Expressed in acid equivalents. The LOQ is 0.05 ppm.
4 The two results for each field trial represent two samples taken from a single plot, not two plots.

TABLE C.4. Summary of Residue Data from Alfalfa Field Trials with Endothall Monoalkylamine Salt (SC/L).

Commodity	Total Applic. Rate[1]	PHI (days)	Residue Levels (ppm)[2]						
			N	Min.	Max.	HAFT[3]	Median (STMdR)	Mean (STMR)	Std. Dev.
Forage	5 ppm (5.94-6.58)	0	2	1.77	2.12	2.12	1.95	1.95	0.25
Hay		0	2	4.93	5.20	5.20	5.07	5.07	0.19

1 The value in parentheses is the total application rate in terms of lb ae/A.
2 Residues are expressed in terms of the free acid. The LOQ is 0.05 ppm.
3 HAFT = Highest Average Field Trial.

D. CONCLUSION

The available field trial data are adequate and support the use of endothall-treated water for irrigation of alfalfa. The data support the use of endothall in irrigation water at a concentration of 5 ppm ae, with no more that six applications per season, and a minimum 7-day interval between applications to the water. Residues in the alfalfa are determined at a 0-day PHI.

E. REFERENCES

None

F. DOCUMENT TRACKING

RDI: David Soderberg (5 June 2009); William Donovan (5 June 2009)
Petition Number: 8E7419
DP#: 356315
PC Code: 038901 and 038905

Template Version June 2005